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## Table of Contents.





## A COMPARISON OF THE BLOOD GROUPS, SUBGROUPS, M–N AND Rh TYPES FOUND IN JAVA WITH THOSE FOUND IN OTHER PARTS OF INDONESIA, TOGETHER WITH A SUMMARY OF THE EVIDENCE FOR NORTH–SOUTH GRADIENTS IN THE VALUES FOR THE BLOOD GENES *q*, *m*, AND $R^1$.


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THE results of the first blood survey on Indonesians conducted from these laboratories were reported by Simmons, Graydon and Ouwehand (1945). A total of 296 individuals who originated in Java, Celebes, Ambon, Timor and 16 other islands was tested for blood groups, subgroups and M–N types. The samples were also classified as Rh-positive or Rh-negative by means of one anti-$Rh_0$ (anti-D) serum for preliminary tests, together with another serum for checking. This second serum was later proved to be anti-$Rh_0rh'$ (anti-D+C). The findings were tabulated according to the island of origin of the individuals. The absence of subgroup $A_2$ was demonstrated, and the M–N percentages found were interesting, because previously published data of other investigators (1934) were considered to be statistically unreliable. Of the 296 samples tested, 294 were regarded as Rh-positive. One sample, which was negative with anti-$Rh_0$ serum but positive with anti-$Rh_0rh'$ serum, was included at that time in the Rh-positive group.

Another point of interest was that the frequencies of the blood groups in Java, where *q* the gene for group B was highest, and *r* the gene for group O was lowest, differed from those found in other parts of Indonesia. A further difference was seen in the M–N frequencies, where gene *m* was highest in Java and gene *n* highest in other islands. These differences suggested that the racial complexes represented in Java and the other island groups of Indonesia were not identical.

In a second survey (Simmons and Graydon, 1947), consisting of two series referred to as series II and series III in their tables, 100 samples were Rh-typed by the use of three anti-Rh sera, and a further 100 samples were Rh-typed by the use of three anti-Rh sera and one anti-hr serum. Results of the tests on the 200 samples were presented, but the figures relative to Java were not separated from those obtained for other islands. The calculated Rh gene frequencies on the pooled samples were as follows: $R^1$ ($R^{o\prime}$) = 0·80, $R^2$ ($R^{o\prime\prime}$) = 0·13, $R^o$ = 0·06, $R^z$ = 0·02.

During 1947 a further series of 105 Javanese blood samples were obtained, and these were subjected to tests for the blood groups, subgroups, M–N types and Rh types. Some of the samples were tested for the Lewis ($Le^a$) blood group.

The purpose of this paper is to present the findings and to combine them with the results of the three earlier series in the same tables for easier reference, and to compare in tabular form blood gene frequencies found by us for various races of the Pacific area. Tables presented show the blood group results pertaining to Java and those relative to miscellaneous Indonesians from 20 other islands. Another table shows the blood group, M–N type and Rh type frequencies relative to various Pacific races. A rearrangement of certain gene frequencies is made to show the evidence available indicating north-south gradients in gene values, and lastly a summary is given of the races tested by us for the $A_1$–$A_2$ subgroups of group A.

The East Indies are the present homeland of the Malay[1] peoples. Two distinct types of Malay stock can be seen in the islands. The so-called "proto-Malays", who are common

[1] The Malays are a religious group not belonging to any one racial or ethnological classification. The terms proto-Malay and deutero-Malay are therefore open to criticism on this score. We have used them, as have others, merely to distinguish two large divisions in the Malayan peoples of Indonesia.

TABLE Ia.

*Blood Groups and M-N Types in Indonesians. Summary of Three Surveys. Javanese.*

| Population. | Authors. | Number of Blood Samples Tested. | Blood Group. | | | | Gene Frequencies. | | | M-N Types. | | | Gene Frequencies. | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | O | $A_1$ | B | $A_1B$ | *p* | *q* | *r* | M | MN | N | *m* | *n* |
| Javanese .. | Simmons, Graydon and Ouwehand (1945). | 107 | 45 (42·1%) | 27 (25·2%) | 27 (25·2%) | 8 (7·5%) | 0·172 | 0·172 | 0·649 | 51 (47·7%) | 44 (41·1%) | 12 (11·2%) | 0·682 | 0·318 |
| Javanese .. | Simmons and Graydon (1947). | 50 | 22 (44%) | 14 (28%) | 12 (24%) | 2 (4%) | 0·19 | 0·16 | 0·66 | 18 (36%) | 22 (44%) | 10 (20%) | 0·58 | 0·42 |
| Javanese .. | This survey. | 105 | 41 (39·0%) | 27 (25·7%) | 30 (28·6%) | 7 (6·7%) | 0·180 | 0·198 | 0·625 | 40 (38·1% | 47 (44·8%) | 18 (17·1%) | 0·605 | 0·395 |
| Total .. | .. .. .. .. | 262 | 108 (41·2%) | 68 (26·0%) | 69 (26·3%) | 17 (6·5%) | 0·178 | 0·180 | 0·642 | 109 (41·6%) | 113 (43·1%) | 40 (15·3%) | 0·632 | 0·368 |

to the interior districts and highlands, are descended from peoples of the earlier Malay immigrations. They have many Caucasoid features, suggesting that they have some racial components in common with the "whites" and Hindus. Later immigrations also from south-eastern Asia consisted of peoples with characteristic mongoloid features, slanting eye with inside fold on the upper lid, and prominent cheek bones. The "deutero-Malay" type can be seen in the coastal districts.

Long before these Malayan groups spread down from Asia other human stocks had settled in the Indies. One of the earliest was from a people characterized by beetling brows, hairy bodies, prognathism and other coarse features. Evidence of persons of this type, who are usually referred to as Australoid or Australomorphic, can still be found in the islands nearer Australia. Probably earlier still was a Negrito type, which still survives in eastern Sumatra, Timor, Alor, the Andaman Islands, Malaya, the Philippines and some of the more inaccessible mountain districts of New Guinea (Kennedy, 1943). There is also evidence that other races have lived at some time or other in the Indies. For instance, there is still to be seen in the Timor-Flores area evidence of a tall, spare-framed, bushy-haired Melanesian type, and there is ample evidence that the Polynesians entered the Pacific after a stay in Java, though they do not apppear to have left any appreciable component in the Indies.

The exact order in which the various migrations took place is not known, nor is the extent to which they have influenced the genetic composition of the present-day inhabitants of the islands.

While many different inferences can be drawn from the physical characteristics observed in the peoples of Indonesia, it is obvious that their genetic composition must be greatly complicated by admixture over many centuries of several racial types. Repeated intrusions by different groups have added further to the complexity and have also tended to prevent the establishment of genetic equilibrium.

The aims of such investigations as the present one are to determine the frequency of occurrence of different blood genes in racial groups, and the frequency of such genes in races considered to be related and those unrelated, and finally, to consider the findings in relation to the racial data already provided by the physical anthropologists and ethnologists. Blood serology covering many identifiable genes is a comparatively new tool in racial investigations. The true value of such work will not be fully known until many investigations have been made in different parts of the world, and the results correlated. To date it can be said that the findings show promise of being most useful, and that a close alliance between the physical anthropologist and the serologist is rapidly becoming a reality.

The data presented in this paper relative to the Indonesians were considered adequate at the time when the investigations were made; but, as has happened in this case, subsequent discoveries of "new" blood genes tend to render each investigation incomplete long before it is published. Another real factor, at present limiting the scope of such surveys, is that the human sera by which "new" blood antigens may be identified are almost invariably extremely rare and therefore in very short supply. Published data concerning recent discoveries of "new" genes and variants have been reviewed by Simmons and Graydon (1950).

## Materials and Methods.

The 105 blood samples were collected on tea plantations in Malaya from Javanese labourers who claimed to be pure Javanese, under the auspices of Dr. John Field, Institute for Medical Research, Kuala Lumpur. The samples were

TABLE Ib.

*Indonesians, Miscellaneous (20 Other Islands).*

| Island. | Authors. | Number of Blood Samples | Blood Groups. | | | | Gene Frequencies. | | | M-N Types. | | | Gene Frequencies. | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | O | $A_1$ | B | $A_1B$ | *p* | *q* | *r* | M | MN | N | *m* | *n* |
| Celebes (Menado). | Simmons, Graydon and Ouwehand (1945). | 47 | 33 (70%) | 6 (13%) | 7 (15%) | 1 (2%) | 0·07 | 0·08 | 0·84 | 8 (17%) | 23 (49%) | 16 (34%) | 0·41 | 0·59 |
| Ambon .. | | 43 | 22 (51%) | 16 (37%) | 5 (12%) | 0 (0) | 0·22 | 0·08 | 0·72 | 8 (19%) | 25 (58%) | 10 (23%) | 0·48 | 0·52 |
| Timor .. | | 38 | 22 (58%) | 5 (13%) | 10 (26%) | 1 (3%) | 0·08 | 0·16 | 0·76 | 6 (16%) | 17 (45%) | 15 (39%) | 0·38 | 0·62 |
| Sixteen other islands. | | 61 | 31 (51%) | 13 (21%) | 14 (23%) | 3 (5%) | 0·14 | 0·15 | 0·71 | 17 (28%) | 26 (43%) | 18 (30%) | 0·49 | 0·51 |
| Eighteen islands. | Simmons and Graydon (1947). | 50 | 22 (44%) | 10 (20%) | 15 (30%) | 3 (6%) | 0·14 | 0·20 | 0·66 | 6 (12%) | 27 (54%) | 17 (34%) | 0·39 | 0·61 |
| Total .. | .. .. .. .. | 239 | 130 (54·4%) | 50 (20·9%) | 51 (21·3%) | 8 (3·3%) | 0·130 | 0·133 | 0·737 | 45 (18·8%) | 118 (49·4%) | 76 (31·8%) | 0·435 | 0·565 |

collected from finger punctures by means of sterile pipettes, and the blood was added to small stoppered bottles of sterile glucose-citrate blood preserving fluid (Simmons and Graydon, 1945). They were then despatched to Singapore packed in an ice-box, and there repacked in iced "Thermos" flasks and air-freighted to Melbourne. The arrangements in Singapore were kindly made by Professor R. G. Scott-McGregor, College of Physicians, Singapore. The blood samples were received in Melbourne in perfect condition and were tested ten days after collection by slide techniques as described in earlier papers of this series, but more recently elaborated by Simmons (1949) and Simmons and Graydon (1950).

TABLE IIA.

*The RH Types in Indonesians. Summary of Three Surveys.*

| Island. | Authors. | Number of Blood Samples Tested. | Anti-$Rh_0$ (Anti-D) Positive.[1] | Percentage. |
|---|---|---|---|---|
| Java .. .. | Simmons, Graydon and Ouwehand (1945). | 107 | 106 | 99 |
| Sixteen other islands. | | 61 | 61 | 100 |
| Celebes (Menado) | | 47 | 45 | 96 |
| Ambon .. | | 43 | 43 | 100 |
| Timor .. .. | | 38 | 38 | 100 |
| Total .. | .. .. .. | 296 | 293 | 99·0 |

[1] The test serum was subsequently proved to be pure anti-$Rh_0$, while the check serum was a polyvalent anti-$Rh_0rh'$ serum.

## Results and Discussion.

The results of earlier surveys conducted on Indonesians (Simmons, Graydon and Ouwehand, 1945, and Simmons and Graydon, 1947) are presented in Tables IA, IB, IIA, IIB and IIC, together with the results found in the present survey on 105 Javanese.

Table IA shows the percentages obtained for the A B O groups and M–N types together with the respective gene frequencies for 262 Javanese. Table IB presents similar data for 239 miscellaneous Indonesians who had originated on 20 islands in the Indies. The differences in the gene frequencies between Javanese and Indonesians from other islands observed in the first series published in 1945 are further confirmed and can be clearly seen in the tables.

### *The A B O Blood Groups and Subgroups.*

The frequencies of *p*, the gene for group A, and *q*, the gene for group B, were higher for Javanese than for other Indonesians. The results of the three surveys on Javanese were fairly uniform. The frequencies found for 262 Javanese were as follows: $p = 0{\cdot}178$, $q = 0{\cdot}180$, and $r = 0{\cdot}642$. Bais and Verhoef (1924) tested the blood groups of 1346 Javanese living on Sumatra, and the frequencies found were as follows: $p = 0{\cdot}178$, $q = 0{\cdot}198$ and $r = 0{\cdot}632$ (Boyd, 1939).

These figures are almost identical with our results obtained over twenty years later for Javanese workers in Malaya, which suggests a common origin for both groups; perhaps both belong to the "deutero-Malay" type, though we have no data on this point.

Examination of the blood group frequencies for 239 miscellaneous Indonesians (Table IB) reveals no notable differences, except perhaps the high frequency of group O in Celebes. Apart from this the frequency of *r*, the gene for group O, is remarkably uniform from island to island. The *p* and *q* frequencies are moderately uniform with certain exceptions, such as in Ambon, where *p* is high and *q* is low. The islands referred to in this table are widely scattered and such differences could be expected. The numbers tested in each group are too small for significance to be attached to these findings. There appear to be no other A B O data for Ambon and Timor. In 143 persons of groups A and AB tested in these surveys no example of $A_2$ or $A_2B$ was detected.

### *The M–N Types.*

There is a considerable difference in the *m* and *n* frequencies for Javanese and other Indonesians. The Javanese have a higher *m* frequency, 0·632, while in the miscellaneous group the *n* frequency, 0·565, is the higher. The results shown in Tables IA and IB are generally uniform in each table. It may well be that the peoples of the miscellaneous group have been subjected to a Melanesian influence not evident in the Javanese. For instance, in Timor, the *n* frequency is 0·618, and Timor is close to the area where the highest *n* frequency in the world is found. In fact, the physical appearance of certain types in Timor indicates Melanesian traits (Kennedy, 1943). This influence appears to be borne out by the *m* and *n* frequencies found in the small sample tested.

Three M–N surveys were conducted in Indonesia by Postmus in 1934 (Boyd, 1939), but statistical analysis indicates that his results were unreliable. The MN type frequencies which he obtained in all his surveys, including that on Hollanders, were low, which suggests that the potency of his sera may have been too low to give satisfactory reactions with all heterozygous ("single dose") cells. No other M–N data for Indonesia have been seen.

### *The Rh Types.*

The Rh types of Javanese and other Indonesians are presented in Tables IIA, IIB and IIC. Table IIA shows the results of the first Rh tests made by Simmons *et alii* (1945). At that time it was possible only to determine whether an individual was Rh-positive or Rh-negative. A total of 296 individuals were tested with an anti-$Rh_0$ (anti-D) serum, and of these 293 (99%) were Rh-positive. One of the three remaining samples was positive with an anti-$Rh_0rh'$ (anti-D+C) serum and the other two failed to react.

TABLE IIB.

*Javanese.*[1]

| Island. | Authors. | Number of Blood Samples Tested. | Anti-$Rh_0$ (Anti-D) Positive. | Percentage. | $Rh_1$. | | $Rh_2$. | $Rh_1Rh_2$. | | $Rh_0$. | $rh'rh''$. |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | $Rh_1Rh_1$. | $Rh_1Rh_0$. | | $Rh_1Rh_2$. | $Rh_1Rh_2$. | | |
| Java .. .. | Simmons and Graydon | 50 | 49 | 98 | 36 | | 0 | 13 | | 0 | 1 |
| Java .. .. | (1947). | 50 | 50 | 100 | 32 | 6 | 1 | 9 | 1 | 1 | 0 |
| Java .. .. | This survey. | 105 | 105 | 100 | 77 | 11 | 1 | 14 | 2 | 0 | 0 |
| Total .. | .. .. .. .. | 155 | | | 109<br>70·3% | 17<br>11·0% | 2<br>1·3% | 23<br>14·8% | 3<br>1·9% | 1<br>0·6% | 0 |
| Grand total | .. .. .. .. | 205 | | | 162<br>79·0% | | 2<br>1·0% | 39<br>19% | | 1<br>0·5% | 1<br>0·5% |

[1] Gene frequencies: $R^1 = 0{\cdot}837$, $R^2 = 0{\cdot}086$, $R^0 = 0{\cdot}065$, $R^z = 0{\cdot}012$.

TABLE IIc.

*Indonesians, Miscellaneous (20 Other Islands).*[1]

| Island. | Authors. | Number of Blood Samples Tested. | Anti-$Rh_0$ (Anti-D) Positive. | Percentage. | $Rh_1$. | | $Rh_2$. | $Rh_1Rh_2$. | | $Rh_0$. | rh'rh". |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | $Rh_1Rh_1$. | $Rh_1Rh_2$. | | $Rh_1Rh_2$. | $Rh_1Rh_2$. | | |
| Twenty islands .. | Simmons and Graydon (1947). | 50<br>50 | 50<br>50 | 100<br>100 | 39<br>32 | 3 | 2<br>2 | 9<br>11 | 2 | 0<br>0 | 0<br>0 |
| Total .. | .. .. .. .. .. | 100 | | | 74<br>74% | | 4<br>4% | 22<br>22% | | 0 | 0 |
| Grand total | .. .. .. .. | 601 | 597 | 99·3% | | | | | | | |

[1] Gene frequencies: $R^1 = 0·81$, $R^2 = 0·13$, $R^0 = 0·04$, $R^z = 0·02$.

Table IIB shows the Rh types of 205 Javanese, and of these all except 50 samples were tested with anti-$Rh_0$, anti-rh', anti-rh" and anti-hr' sera. The 50 samples referred to were tested with three anti-Rh sera only. The Rh phenotypes show mainly that 79% were of type $Rh_1$ and that types $Rh_1Rh_2$ and $Rh_0$ were detected. The Rh gene frequencies calculated from the type percentages were as follows: $R^1 = 0·837$, $R^2 = 0·086$, $R^0 = 0·065$, $R^z = 0·012$.

In the calculation of these frequencies the solitary example of rh'rh" was omitted. However, this case was carefully rechecked and the reactions were confirmed. To explain the occurrence of this rare phenotype we must postulate the existence in this race of two extra genes, $r'$ and $r''$, or of the gene $r^y$, which is extremely rare in white populations. We have no means of distinguishing between the genes $r^y$ and $R^z$ in three other samples in which either one or the other has been found. Therefore it may be no more unreasonable to ascribe the observed phenotype rh'rh" to the chance occurrence of the genotype $r'r^y$ than to chance simultaneous appearance of genes $r'$ and $r''$, neither of which has appeared elsewhere in our series. On the other hand, it should be borne in mind that the latter genes, if present, would be detected only in phenotypes rh'rh', rh'rh", rh"rh", all of which would occur but rarely unless the frequencies of the genes $r'$ and $r''$ were relatively high. Throughout the text of this paper we have referred to the presence of gene $R^z$ where the reactions indicate that either $R^z$ or $r^y$ may be present.

Table IIc shows the Rh types of 100 Indonesians selected at random who had originated on 20 islands. One-half had been tested with three anti-Rh sera only, while the others, collected later, were tested with an anti-hr' serum also. The percentage of type $Rh_1$ in this series was 74, and type $Rh_1Rh_2$ was again demonstrated. The gene frequencies calculated from the phenotype percentages were as follows: $R^1 = 0·81$, $R^2 = 0·13$, $R^0 = 0·04$, $R^z = 0·02$.

Comparison between the Rh gene frequencies in Javanese and in miscellaneous Indonesians shows a close similarity. The differences observed in the two groups of people in the A B O and M–N type frequencies were not continued into the Rh types. It might have been expected that the Melanesian influence suggested as the reason for the different A B O and M–N frequencies observed in the miscellaneous Indonesians would have given them an $R^1$ frequency higher than that of the Javanese, for the $R^1$ gene frequency of Melanesians centred around New Guinea is the highest for all races so far tested. North from New Guinea to south-east Asia there is some evidence of a north-south gradient for this gene (*vide infra*).

The Australian aborigines, on the other hand, possess blood group and Rh type frequencies quite distinct from any other coloured race (Simmons and Graydon, 1948). Indians (Moslems) also show a distinctive gene complex (Wiener, Sonn and Belkin, 1945).

A total of 601 Indonesians in all were tested with anti-$Rh_0$ serum, and of these 597 (99·3%) were Rh-positive. Of the four samples found to be anti-$Rh_0$ negative, one from Java was shown to be of type rh'rh", a second from Java gave a positive reaction with a polyvalent anti-$Rh_0$rh' serum, and the remaining two from Celebes gave no reaction with this serum. They could therefore have been of type rh" or Rh-negative (rh).

### *The Lewis (Le$^a$) Blood Group in Javanese.*

Forty group O samples from the last series of 105 Javanese were tested with an anti-Le$^a$ serum of group O, and 16 (40%) gave excellent agglutination. Although we have found that Lewis-positive reactions may be weaker in strength with old cells than with freshly collected cells, the above-mentioned reactions appeared to be clear-cut and reliable.

It will be remembered that examples of anti-Lewis serum are not common, and it is therefore difficult to select or prepare high titre sera as is possible for group, M–N and Rh tests. We have repeatedly demonstrated that sterile samples of blood free from hæmolysis, stored at 5° C. in a suitable blood preservative, give strong and specific group, M–N and Rh reactions for many months after collection. An important limiting factor in agglutination with stored cells is the potency of the testing reagents used. The anti-Lewis serum with which most of our studies have been made was that described by Jakobowicz, Simmons and Bryce (1947). Of six anti-Lewis sera tested, this serum (Mrs. M.P.) gave by far the strongest reactions (Krieger and Simmons, 1949). Reactions were stronger at room-temperature (20° C.) than at 37° C. This serum has now been thoroughly tested and its reliability proved.

Results of investigations in which comparisons were made between Lewis reactions and A-B-O secretor tests in saliva in white Australians by Simmons, Semple and Graydon, are now in the press.

The series of Lewis tests on Javanese in 1947 was small; however, it did indicate that Javanese possess the Lewis antigen in their blood, and in possibly a higher percentage than that found in the white race. The results are presented subject to confirmation when further blood samples can be tested.

### *Comparison of Gene Frequencies in Various Coloured Races.*

A comparison of some of the group ($p$, $q$, $r$), M–N ($m$, $n$) and Rh gene frequencies has been made with a view to obtaining a picture of the progress made in blood gene investigations for various coloured races from China, Japan, Siam, India, and through the East Indies to other races in the south-west Pacific. Where a later survey has confirmed the results of an earlier survey, only the figures for the initial investigation are presented. The summarized results are given in Table III.

Some evidence of directional gradients in the frequencies of certain genes can be seen in these figures. Accordingly the data have been rearranged in Table IV to bring out this evidence more clearly. For this purpose, the frequency of $q$, the gene for group B, is shown in order of magnitude from highest to lowest values. The frequency of $m$, the gene for type M, is arranged similarly. Of the Rh genes,

TABLE III.

*Gene Frequencies in Various Coloured Races of South-Eastern Asia and the Western Pacific.*

| Population. | Authors. | ABO Groups. | | | | M-N Types. | | | Rh Types. | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Number of Samples Tested. | Frequency of Genes. | | | Number of Samples | Frequency of Genes. | | Number of Samples | Frequency of Genes. | | | | | |
| | | | *p* | *q* | *r* | | *m* | *n* | | $R^1$ | $R^2$ | $R^0$ | $R^z$ | r° | r' |
| Chinese[2] (Southern). | Simmons, Graydon, Semple and Green (1950) | 250 | 0·165 | 0·139 | 0·681 | 250 | 0·630 | 0·370 | 250 | 0·760 | 0·195 | 0·040 | 0·005 | 0 | 0 |
| Japanese .. | Graydon, Simmons *et alii* (1945). | 400 | 0·274 | 0·175 | 0·555 | 400 | 0·540 | 0·460 | 400 | 99·5% | anti-R | $h_s$ | positive | | |
| Japanese .. | Miller and Taguchi (1945). | 180 | 0·274[1] | 0·176 | 0·543 | | | | 180 | 0·702[2] | 0·277 | 0 | 0 | 0 | 0·021 |
| Siamese .. | Phansomboon, Ikin and Mourant (1949). | 213 | 0·148 | 0·257 | 0·595 | 213 | 0·662 | 0·338 | 213 | 0·755 | 0·112 | 0·111 | 0·022 | 0 | 0 |
| Indians (Moslems .. | Wiener, Sonn and Belkin (1945). | 156 | 0·185 | 0·261 | 0·583 | 156 | 0·622 | 0·378 | 156 | 0·562 | 0·060 | 0·034 | 0 | 0·044 | 0·266 |
| Filipinos .. | Simmons and Graydon (1945). | 382 | 0·152 | 0·181 | 0·671 | 382 | 0·510 | 0·490 | 382 | 99·7% | anti - | $Rh_s$ | positive | | |
| Filipinos .. | Simmons and Graydon (1945). | | | | | | | | 101[4] | 0·88 | 0·08 | 0·03 | 0·01 | 0 | 0 |
| Indonesians (Java). | This survey. | 262 | 0·178 | 0·180 | 0·642 | 262 | 0·632 | 0·368 | 205[5] | 0·837 | 0·086 | 0·065 | 0·012 | 0 | 0 |
| Indonesians (20 other islands). | This survey. | 239 | 0·130 | 0·133 | 0·737 | 239 | 0·435 | 0·565 | 100 | 0·81 | 0·13 | 0·04 | 0·02 | 0 | 0 |
| Indonesians .. | This survey. | | | | | | | | 601 | 99·3% | anti - | $Rh_s$ | positive | | |
| Papuans[3] .. | Simmons, Graydon *et alii* (1946). | 228 | 0·183 | 0·197 | 0·636 | 228 | 0·039 | 0·961 | | | | | | | |
| Papuans .. | Simmons, Graydon *et alii* (1946). | 227 | 0·215 | 0·127 | 0·674 | 227 | 0·227 | 0·773 | 455 | 100% | anti - R | $h_s$ | positive | | |
| Papuans .. | Simmons and Graydon (1947). | | | | | | | | 100 | 0·943 | 0·020 | 0·021 | 0·016 | 0 | 0 |
| Admiralty Islanders | Simmons and Graydon (1947). | 112 | 0·146 | 0·136 | 0·720 | 112 | 0·339 | 0·661 | 112 | 0·940 | 0·030 | 0·030 | 0 | 0 | 0 |
| Fijians .. | Simmons, Graydon and Barnes (1945). | 200 | 0·225 | 0·120 | 0·660 | 200 | 0·332 | 0·667 | 200 | 100% | anti - R | $h_s$ | positive | | |
| Fijians .. | Simmons and Graydon (1947). | | | | | | | | 110 | 0·840 | 0·050 | 0·110 | 0 | 0 | 0 |
| New Caledonians, Loyalty and Pine Islanders | Simmons, Graydon and Avias (1949). | 558 | 0·204 | 0·059 | 0·731 | 558 | 0·297 | 0·703 | 558 | 0·833 | 0·107 | 0·054 | 0·004 | 0 | 0 |
| Australian Aborigines[2] | Wilson, Graydon, Simmons and Bryce (1944). | 649 | 0·251 | 0 | 0·749 | 649 | 0·297 | 0·703 | | | | | | | |
| Australian Aborigines. | Simmons and Graydon (1948). | | | | | | | | 234 | 0·564 | 0·201 | 0·085 | 0·021 | 0·129 | 0 |
| Australian Aborigines. | Simmons and Graydon (1948). | | | | | | | | 515 | 99·2% | anti-R | $h_s$ | positive | | |
| Maoris[3] .. | Graydon and Simmons *et alii* (1946) | 267 | 0·352 | 0·004 | 0·642 | 267 | 0·489 | 0·511 | 267 | 100% | anti - R | $h_s$ | positive | | |

[1] A B O frequencies calculated by us.

[2] Rh gene frequencies calculated by Wiener, Zepeda, Sonn and Polivika (1945).

[3] New surveys in progress.

[4] One blood sample additional to the series reported in 1945 proved to be $Rh_1R_z$. Gene frequencies for this group are largely hypothetical, as tests were not performed with anti-hr' (anti-c) sera in this series.

[5] One example of phenotype rh'rh" was found in this series and is referred to in the text.

gene $R^1$ was selected to demonstrate the variations in values found.

Bernstein (1932) drew attention to an east-west gradient in the values of *q*. The highest values were found in the peoples of central Asia and values progressively decreased from east to west across Europe. Further, on movement away from central Asia in any direction, the values of *q* decrease, and it has been shown that in the marginal peoples of the world the value for *q* is zero or extremely small—for example, Australian aborigines, American Indians, Maoris, Eskimos.

Birdsell and Boyd (1939) suggested that there was probably a north-south gradient in values of *m*, and the results of a number of surveys by the present authors support this theory. In Table IV will be seen evidence of a north-south gradient in values both for *q* and for *m*. Examination of the figures for the Rh gene $R^1$ shows that there is evidence of possibly two groupings, mainly on a south-north basis. The highest frequencies of $R^1$ are seen for Papuans, Admiralty Islanders, Filipinos, Fijians, Indonesians and New Caledonians, while a group with somewhat lower values in the north consists of Chinese, Siamese and Japanese. There are, however, two exceptions to this general grouping—the Asiatic Indians of the north and the Australian aborigines of the south. Both races possess an intermediate and almost equal value for $R^1$. They also possess Rh gene characteristics not generally seen in the other races tested. For instance, both Indians and Australian aborigines possess the gene *r'* (also possibly detected in two of 601 Indonesians), and in addition, the Indians alone of all these races tested possess a moderately high frequency of the Rh-negative gene *r*, and subgroup $A_2$. The $R^z$ gene shown to be present in Australian aborigines and a number of the Pacific races has not yet been demonstrated in the Indians. Larger series for each race may be necessary to demonstrate the $R^z$ gene where it has not been found to date. It has been suggested on sound anthropological grounds that there is an appreciable physical component common to the Australian aborigines and some of the Indian peoples: this common component must have been deficient in gene *q* and in subgroup $A_2$; it very likely possessed gene *m* in low frequency and gene *r'* as one of its Rh genes.

Two outstanding characters of American Negroes (Wiener, Belkin and Sonn, 1944) are the frequencies of gene $R^0$ and subgroup $A_2$, both the highest in races tested to date. These same characters are respectively of low frequency and entirely absent in the Pacific races referred to in this paper. Because of certain physical characteristics some of the Pacific races, particularly the Melanesians, are sometimes referred to as Oceanic Negroes. No evidence of relationship between the African (or American) Negro and the Melanesian can be drawn from the blood gene frequencies, and it seems most unlikely that they have any appreciable component in common.

TABLE IV.

*Evidence for North-South Gradients in the Values of q, m and $R^1$ Genes in Various Coloured Races.*

| Gene *q*. | | Gene *m*. | | Gene $R^1$. | |
|---|---|---|---|---|---|
| Indians (Moslems) | 0·261 | Siamese | 0·662 | Papuans | 0·943 |
| Siamese | 0·257 | Indonesians (Java) | 0·632 | Admiralty Islanders | 0·94 |
| Filipinos | 0·181 | Chinese (Southern) | 0·630 | Filipinos | 0·88 |
| Indonesians (Java) | 0·180 | Indians (Moslems) | 0·622 | Fijians | 0·84 |
| Japanese | 0·175 | Japanese | 0·540 | Indonesians (Java) | 0·837 |
| Papuans | 0·197 / 0·127 | Filipinos | 0·510 | Indonesians (20 islands) | 0·81 |
| | 0·167 | Maoris | 0·489 | New Caledonians, Loyalty and Pine Islanders | 0·833 |
| Chinese (Southern) | 0·139 | Indonesians (20 islands) | 0·435 | | |
| Admiralty Islanders | 0·136 | Loyalty Islanders | 0·386 | Chinese (Southern) | 0·76 |
| Indonesians (20 islands) | 0·133 | Admiralty Islanders | 0·339 | Siamese | 0·755 |
| Fijians | 0·120 | Pine Islanders | 0·333 | Japanese | 0·702 |
| New Caledonians | 0·059 | Fijians | 0·332 | | |
| Pine Islanders | 0·041 | New Caledonians | 0·297 | Australian Aborigines | 0·564 |
| Loyalty Islanders | 0·025 | Australian Aborigines | 0·297 | Indians (Moslems) | 0·562 |
| Maoris | 0·004 | Papuans | 0·039 / 0·227 | | |
| Australian Aborigines | 0 | | 0·133 | | |

### *The $A_1$-$A_2$ Subgroups of Group A.*

Table V presents the collected results of the $A_1$-$A_2$ tests made by us on various races. The significant feature is the absence, or extreme rarity, of subgroup $A_2$ in the coloured races of the Pacific. In white Australians and Hollanders, subgroup $A_2$ occurs in 22% and 23% respectively of those individuals found to be of group A. The virtual absence of $A_2$ has also been demonstrated in Hawaiians, American Indians, Eskimos and possibly others. The two coloured races which are the main exceptions to the above rule are the American Negroes and Asiatic Indians. In the former the percentage of $A_2$ is extremely high in relation to the numbers found to be of group A, and in the latter the percentage is much lower than that found in the white race.

The results of other surveys carried out on further coloured racial groups in the Pacific are now being prepared for publication. In each series the absence of $A_2$ is again a feature.

It will be seen that subgroup $A_2$, like other blood factors, will play its part in the progressive elucidation of racial origins.

The results presented in this paper show sound evidence of the progress being made in blood genetics of race. From the point of view of the investigator the task appears to be never ending, as the discovery of each "new" blood antigen and its corresponding antibody means that new surveys should be undertaken. At the time of writing this paper we are using over 20 antisera for testing, and a large portion of these sera are distinct types. Duplication in the use of antisera of certain types occurs only in the search for variants at a particular gene locus, or in the testing of certain blood samples for confirmation of results.


### Acknowledgements.

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### Summary.

1. The blood groups and M–N and Rh types of a further 105 Indonesians from Java have been determined, making a total of 262 Javanese tested.

2. The group percentages were as follows: group O, 41·2; group A, 26·0; group B, 26·3; group AB, 6·5. All the 85 individuals of groups A and AB were found to belong to subgroups $A_1$ and $A_1B$ respectively. Gene frequencies calculated from these figures were as follows: $p = 0{\cdot}178$, $q = 0{\cdot}180$, $r = 0{\cdot}642$.

3. The M–N type percentages were: type M, 41·6; type MN, 43·1; type N, 15·3. From these the gene frequencies $m = 0{\cdot}632$ and $n = 0{\cdot}368$ were calculated.

4. Rh typing carried out on 205 Javanese showed that 79% were of phenotype $Rh_1$, 1% of phenotype $Rh_2$, 19% of phenotype $Rh_1Rh_2$, 0·5% of phenotype $Rh_0$ and 0·5% of


TABLE V.

*The $A_1$-$A_2$ Subgroups found in Various Races by the Present Authors and Various Co-Workers.*

| Population.[1] | Authors. | Number of Blood Samples Tested. | | Subgroups of Group A Found. | | | |
|---|---|---|---|---|---|---|---|
| | | Group A. | Group AB. | $A_1$. | $A_2$. | $A_1B$. | $A_2B$. |
| Australian Aborigines | Simmons, Graydon and Hamilton (1944). | 105 | 0 | 105 | 0 | 0 | 0 |
| Australian Aborigines | Wilson, Graydon, Simmons and Bryce (1944). | 293 | 0 | 293 | 0 | 0 | 0 |
| Australian Aborigines | Simmons and Graydon (1948). | 20 | 1 | 20 | 0 | 1 | 0 |
| Indonesians | Simmons, Graydon and Ouwehand (1945) | 67 | 13 | 67 | 0 | 13 | 0 |
| Indonesians | Simmons and Graydon (1947). | 24 | 5 | 24 | 0 | 5 | 0 |
| Indonesians | Simmons and Graydon (present survey). | 27 | 7 | 27 | 0 | 7 | 0 |
| Fijians | Simmons, Graydon and Barnes (1945) | 68 | 12 | 68 | 0 | 12 | 0 |
| Fijians | Simmons and Graydon (1947). | 32 | 5 | 32 | 0 | 5 | 0 |
| Japanese | Graydon, Simmons, Heydon and Bearup (1945). | 149 | 40 | 149 | 0 | 38 | 2 |
| Papuans | Graydon and Simmons (1945). | 57 | 14 | 57 | 0 | 14 | 0 |
| Papuans | Simmons, Graydon and Woods (1946). | 68 | 24 | 68 | 0 | 24 | 0 |
| Filipinos | Simmons and Graydon (1945). | 84 | 23 | 83 | 1 | 23 | 0 |
| Maoris | Graydon, Simmons *et alii* (1946). | 155 | 0 | 155 | 0 | 0 | 0 |
| Admiralty Islanders | Simmons and Graydon (1947). | 26 | 4 | 26 | 0 | 4 | 0 |
| New Caledonians, Loyalty and Pine Islanders. | Simmons, Graydon and Avias (1949). | 190 | 20 | 190 | 0 | 20 | 0 |
| Chinese | Simmons, Graydon, Semple and Green (1950). | 63 | 19 | 63 | 0 | 19 | 0 |
| White Australians | Simmons, Graydon, Jakobowicz and Bryce (1943). | 1292 | — | 1008 (78%) | 284 (22%) | — | — |
| Hollanders | Graydon, Simmons, Woods and Lumkeman (1946). | 79 | 10 | 61 (77%) | 18 (23%) | 9 | 1 |

[1] Papers relative to other racial groups in the Pacific are now in preparation.

phenotype rh'rh". The gene $R^z$ (or $r^y$) was demonstrated. From these figures the gene frequencies $R^1$ = 0·837, $R^2$ = 0·086, $R^0$ = 0·065, $R^z$ = 0·012, were calculated.

5. The results of tests for blood groups and M–N and Rh types in several series of Indonesians totalling 239 from 20 other islands have been compiled separately.

6. The group percentages were as follows: group O, 54·4%; group A, 20·9%; group B, 21·3%; group AB, 3·3%. All the 58 individuals of groups A and AB were found to belong to subgroups $A_1$ and $A_1B$ respectively. Gene frequencies calculated from these figures were as follows: $p$ = 0·130, $q$ = 0·133, $r$ = 0·737.

7. The M–N type percentages were: type M, 18·8%; type MN, 49·4%; type N, 31·8%. From these the gene frequencies $m$ = 0·435 and $n$ = 0·565 were calculated.

8. Rh typing carried out on 100 of these individuals showed that 74% were of phenotype $Rh_1$, 4% were of phenotype $Rh_2$ and 22% were of phenotype $Rh_1Rh_2$. The gene $R^z$ (or $r^y$) was again demonstrated. From these figures the gene frequencies $R^1$ = 0·81, $R^2$ = 0·13, $R^0$ = 0·04, $R^z$ = 0·02, were calculated.

9. A total of 601 Indonesians in all were tested with anti-$Rh_0$ (anti-D) serum, and of these 597 (99·3%) were Rh-positive. Of the four samples found to be anti-$Rh_0$ negative, one from Java proved to be of type rh'rh", another from Java was positive with an anti-$Rh_0$rh' serum, while two samples from Celebes failed to agglutinate with this polyvalent serum, and therefore could have been of type rh" or Rh-negative, rh.

10. Forty group O samples from the last series of 105 Javanese were tested with an anti-$Le^a$ (Lewis) antiserum, and 16 (40%) gave excellent agglutination. The reliability of Lewis reactions with old but suitably preserved blood is discussed.

11. The blood gene frequencies found in Javanese are compared with those found in miscellaneous Indonesians who had originated on 20 other islands.

12. A comparison has been made of the values for genes $p$, $q$, $r$, $m$ and $n$, and the various Rh genes found in a number of coloured races in Asia and the Pacific Ocean area.

13. Evidence has been collected in tabular form showing north-south gradients in the values for the genes $q$, $m$, and $R^1$ in the same coloured races.

14. A table has been compiled which summarizes our $A_1$-$A_2$ results for various races.

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## SYSTEMIC MYCOSIS DUE TO MONILIA ALBICANS.[1]


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IN the following pages the older and better known generic name "Monilia" has been used instead of the name "Candida", as the disease caused by members of the genus is still called "moniliasis".

As *Monilia albicans*, with which we are here concerned, has so frequently been isolated from the fæces, vagina, skin and pharynx of apparently normal people, and as it occurs commonly as a secondary invader in many bronchopulmonary conditions, confusion as to its pathogenicity has arisen. However, the clinical and pathological entities of cutaneous, vaginal, pharyngeal and bronchopulmonary moniliasis are now well recognized. More recently, fatal œsophageal moniliasis has been described in infants of low vitality and causing a discrete clinical picture resembling that of pyloric stenosis. Ebbs (1938) found that 22 out of 28 cases of œsophagitis occurring over a period of three years were due to *Monilia albicans*. Reye (1941) reported five cases of monilial œsophagitis occurring in 150 consecutive necropsies. Ludlam and Henderson (1942) found that in a series of 18 necropsies, spread to the œsophagus from the pharynx had occurred in seven cases. Lederer and McLaren Todd (1949), in 204 necropsies on infants aged under twelve months, encountered 26 cases of pharyn-

[1] Read at a meeting of the Section of Pathology, Bacteriology, Biochemistry and Experimental Medicine, Australasian Medical Congress (British Medical Association), Seventh Session, Brisbane, May-June, 1950.

geal or œsophageal thrush, in all of which the condition was directly or indirectly the cause of death.

Rare cases of monilial endocarditis occurring almost exclusively in drug addicts have been reported, the symptomatology and course resembling that of subacute bacterial endocarditis.

Meningitis also is rare. Miale (1943) reports a case confused clinically and histologically with tuberculosis. Pharyngeal granulomata had been present for eight years before the onset of meningitic symptoms.

Monilæmia with mycotic lesions in the viscera, apart from occurring as a terminal event in monilial endocarditis and in pulmonary moniliasis, is very rarely reported. An interesting case is reported by Wiseler and Browne (1945), in which apparent spontaneous recovery occurred in a patient from whom *Monilia albicans* was isolated (blood, urine, fæces and sputum) on several occasions. Vesical lesions were seen on cystoscopic examination and the history was suggestive of bronchopulmonary moniliasis of some years' duration. In the series reported by Lederer and McLaren Todd, two cases of monilæmia with abscesses in the kidney were encountered. One of these was associated with pyæmia due to staphylococci (type not stated).

When four cases of systemic mycosis in infants occurred at the Brisbane Children's Hospital within a period of five months, they were considered worth reporting, firstly because of the rarity of the condition, and secondly because attempts to establish the source of the infection, although not successful, led to some interesting findings and speculations of some practical importance. These four cases all occurred in infants suffering from enterocolitis. The symptoms did not resemble those of monilial œsophagitis.

### Reports of Cases.

The clinical histories and relevant autopsy findings, together with brief cultural and histological findings, are as follows. (The cultural characteristics and histology of the lesions are discussed later.)

CASE I.—J.M.H., a male patient, aged fourteen months, was admitted to hospital on May 28, 1948, with a history of diarrhœa, vomiting and cough, of one week's duration. He was very pale, ill and dehydrated, with numerous moist sounds in the chest. Penicillin (1000 units every three hours) and intravenous therapy (half-strength normal saline and 5% glucose solution) were given immediately. On June 5 it was noted that vomiting and diarrhœa were still present, the temperature was 102° F., the hæmoglobin value was 48%, and the serum protein content was 4·8 grammes *per centum*. The child's condition deteriorated, and death occurred at 9.10 a.m. on June 16.

The autopsy was performed about one hour after death. No oral or œsophageal thrush was found. The lower lobe of the left lung contained a large confluent area of consolidation. Both kidneys were greatly enlarged and contained numerous miliary abscesses. The mesenteric glands were enlarged and injected and the small bowel was slightly injected.

*Bacillus friedländeri* was grown on culture from the lung, *Monilia albicans* was obtained in pure culture from the kidney, and Salmonella (Group B) was grown from contents of the large and the small bowel.

Owing to a misunderstanding the kidneys only were preserved for section; numerous mycotic abscesses were found in the cortex and medulla.

CASE II.—R.B.M., a male infant, aged eleven months, was admitted to hospital on September 30, 1948, with a history of diarrhœa and vomiting of six days' duration. He had had pneumonia nine months previously. Diarrhœa and vomiting continued after his admission to hospital, and intravenous therapy (5% glucose solution, half-strength normal saline and later parenamine) was commenced on October 3. Moist sounds were noted in the chest on October 11 and the intramuscular administration of penicillin was commenced. A bilateral mastoidectomy was performed on October 18. The presence of oral thrush was noted on October 20. Continuous pyrexia (temperature 102° F.) and signs of pneumonia, diarrhœa and vomiting persisted till the child's death on October 24 at 10.45 a.m.

The autopsy was performed twenty-three hours after death. Severe oral and pharyngeal thrush extending to the upper third of the œsophagus was present. There were confluent areas of consolidation in the lower lobes of both lungs. The heart was normal in size, but throughout the myocardium were numerous yellowish pin-head abscesses; the valves were normal. Localized thrombophlebitis was present in all veins used for transfusion (that is, in both antecubital fossæ and over the medial malleoli). In the liver gross fatty change was found. Both kidneys were enlarged and swollen (the right weighed three ounces, the left three and a half ounces), and the parenchyma was thickly studded with small yellowish abscesses, most numerous in the cortex. The pelvis, ureters and bladder were normal. Numerous minute areas of ulceration with hæmorrhagic margins were present in the mucosa of the transverse and descending colon. The remainder of the alimentary tract was normal.

*Hæmophilus influenzæ* was isolated from the lungs, and *Monilia albicans* was grown in pure culture from the pharynx, kidneys and heart. No pathogens were isolated from the contents of the small and large intestine.

Mycotic abscesses were present in the kidneys and myocardium; there was superficial mycosis only on the pharynx and the upper part of the œsophagus. Of the four veins (portions taken from sites of venoclysis), examination of three revealed thrombosis and some recanalization, and in one septic thrombosis was found with numerous spores and mycelial threads, some perforating the wall of the vein. There was proliferation of the fungus in the surrounding areolar tissue without cellular reaction (possibly post-mortem growth). Examination of the colon revealed superficial ulceration and lymphoid hyperplasia. No fungus could be seen.

CASE III.—M.G., a male patient, aged seven months, had had diarrhœa with blood-stained stools for four days before his admission to hospital on November 1, 1948, and vomiting for one day. Intravenous therapy (half-strength normal saline and 5% glucose solution and one blood transfusion) was commenced on November 11. The intramuscular administration of penicillin was commenced next day when *otitis media* was noted, and a bilateral mastoidectomy was performed on November 18. The infant's condition deteriorated, diarrhœa and vomiting persisted, abdominal distension was noted on November 21, and death occurred on November 23 at 8.10 p.m.

The autopsy was performed fourteen hours later. The lungs and the heart and its valves were normal. In the liver severe fatty degeneration was present. Both kidneys were enlarged and swollen and contained numerous small white abscesses. There was considerable bullous emphysema of the intestines, and the lower part of the ileum and the colon were inflamed. The remainder of the alimentary tract was normal.

Salmonella (group C) and *Monilia albicans* were grown on culture from the contents of the small and large intestine. *Monilia albicans* was isolated in pure culture from the heart and kidneys.

Mycotic abscesses were present in the kidneys and myocardium (very rare) on section. Large empty bullous spaces were present in the submucosa of the ileum and colon, the mucosa was infiltrated by chronic inflammatory cells and no fungus was found. Two veins on section showed thrombosis and recanalization; one showed great thickening of the media and adventitia, which were heavily infiltrated by lymphocytes and plasma cells; the thrombus in the lumen contained numerous polymorphonuclear cells and many spores and mycelial elements, which in some places had penetrated to the media.

CASE IV.—M.G.D., a male patient, aged five months, was admitted to hospital on October 25, 1948, with a history of diarrhœa present for three days and vomiting for one day. Intravenous therapy (saline and 5% glucose solution) was commenced on November 1. He was pyrexial on November 2; next day the left leg at the site of venoclysis was noted to be infected and the drip apparatus was removed; but as diarrhœa and vomiting continued, intravenous therapy was recommenced on November 9. Bilateral mastoidectomy was performed on November 12. The abdomen became distended three days later, and death occurred on November 23 at 4.30 p.m.

The autopsy was performed seventeen hours later. In both lungs areas of consolidation were present, confluent in the lower lobes. The heart and its valves were normal, and no oral or œsophageal thrush was found. In the liver gross fatty change was present. Both kidneys were enlarged and contained a few scattered necrotic lesions, mostly in the cortex. The mesenteric glands were enlarged and injected, the colonic mucosa was very inflamed, and there was bullous emphysema of the wall of the small bowel and colon.

*Pseudomonas pyocyanea*, *Salmonella* (group B) and *Monilia albicans* were isolated from the small and large bowel. *Monilia albicans* in pure culture was isolated from the heart and kidneys.

Very scanty mycotic abscesses were present in sections of kidneys and myocardium. Sections were prepared of one vein only, and thrombosis and organization only were found. In the lungs bronchopneumonia only was present; no fungus was found.

### Cultural Characteristics.

*Monilia albicans* is the only species pathogenic for laboratory animals. Rabbits injected intravenously with the fungus die in four or five days with swollen kidneys containing numerous small white mycotic abscesses which may also be present under the endocardium and pleura and in the liver.

The fungus grows well at room temperature and at 37° C. on media containing glucose and on blood agar. The cultural requirements appear to be few, glucose being the most important. Aerobic conditions cause the development of a yeast-like growth, but some degree of anaerobiasis causes the development of mycelium.

Chlamydospore production forms an easy method of identifying *Monilia albicans* (other species do not develop chlamydospores).

The media used for identification and culture by us were Sabouraud's glucose agar, glucose broth and blood agar. The production of chlamydospores was observed in corn meal extract containing 0·05% Congo red (Anderson, 1946); this dye is taken up partly by the mycelium, but mostly by the chlamydospores. As the sugar reactions reported in the literature are variable, glucose, maltose, sucrose and lactose only were used. The results obtained are shown in Table I. Unfortunately, at the time no rabbits were available for intravenous injection.

### Histological Findings in the Lesions.

The fungus appears as small, oval, budding, thin-walled, yeast-like cells 2·0$\mu$ to 4·0$\mu$ in diameter; mycelial elements may be present and are 2·0$\mu$ to 3·0$\mu$ thick; blastospores show a thin doubly refractile capsule and are easily identified if they occur in clusters. The fungus does not stain well in hæmatoxylin and eosin preparations—often it does not stain at all; on the other hand, the spores may be mistaken for lymphocytes. However, lowering the condenser a little shows up the refractile spores and mycelium clearly. If Gram's stain is used the spores are generally Gram-positive and the mycelium has an irregularly beaded appearance. The stains used for sections in the four cases described above were hæmatoxylin and eosin and MacCallum's modification of Goodpasture's method.

In sections the lesions usually appear as central radiating strands of mycelium and spores with a surrounding cellular reaction—usually lymphocytes, large mononuclear cells and some polymorphonuclear cells. There is usually increased vascularity. Giant cells may be present.

Miale (1941) described (and illustrated) in his case granulomatous lesions in the pharynx and meninges confused with tuberculosis. These showed central necrosis and surrounding epithelioid and giant-cell reaction. Blastospores were observed in the giant cells of the meningitic lesions, and a review of the ante-mortem biopsy material from the pharynx showed the presence of spores and mycelium when Gram's stain was used.

Fuente's method (1945), in which a fat stain and frozen sections are employed, has not been tried here in Brisbane.

In the material obtained from our four cases the lesions were irregularly rounded and consisted of a central core of necrotic parenchyma containing radiating strands of mycelium and spores, surrounded by an ill-defined zone of mononuclear cells and a few polymorphonuclear cells. Small "giant cells" of the foreign body type, usually packed with refractile spores, were seen occasionally.

Although it could be argued that the fungus was a post-mortem contaminant, especially as there was a lapse of half to one day after death in three cases before fixation of material, yet in one case a lapse of barely one hour occurred and the presence of a cellular reaction surrounding the fungus seems good evidence for its ante-mortem presence.

It should be noted in these four cases that no mycotic lesions were present on the heart valves (sections in three cases) and in only one case was pharyngeal and œsophageal thrush found *post mortem*. Reye draws attention to the difficulty in macroscopic diagnosis of œsophageal moniliasis, especially if post-mortem digestion of the lower third (the most common site) has occurred.

Lederer and McLaren Todd mention one case in their series in which bullous emphysema of the bowel wall occurred, as it did in two of the above cases (fungus was not present in the sections from any of these).

Gutman (1946) describes a case of associated *Salmonella suipestifer* and monilial infection of the bowel, the fungus showing up in sections of the bowel wall; œsophageal moniliasis was also present.

### Possible Source of Infection in the Four Cases Reported.

*Infection via the Alimentary or Respiratory Tract.*

Lederer and McLaren Todd regard the pharynx or œsophagus as the primary site of infection. Aspiration of infected material may lead to sudden death or to multiplication of the fungus and its spread through the bronchial wall (they give one illustration of this). Spread via the blood-stream in the two cases reported by them may have occurred by invasion of vessels in the pharynx or lung.

Infection of at least some of the infants by contacts (mother, nurses, bed linen and utensils) is suggested by these authors and also by Anderson *et alii* (1944).

In the four cases of the series under discussion, in only one was cultural and histological evidence of pharyngeal and œsophageal moniliasis obtained. It was impossible to trace a source of infection in the ward owing to changes in personnel, and also this did not appear likely. Culture media exposed in the wards on three occasions did not yield *Monilia albicans*.

*Infection via the Intravenous Route.*

The presence of *Monilia albicans* in the thrombus and vein wall in two cases suggest infection via the intravenous

TABLE I.

| Subject. | Glucose Agar. | Glucose Broth. | Blood Agar. | Corn Meal Extract. | Glucose. | Maltose. | Sucrose. | Lactose. |
|---|---|---|---|---|---|---|---|---|
| J.M.H. .. | Creamy colonies. Yeasty smell. | No surface growth. | Medium sized greyish colonies. | Branched mycelium and chlamydospores (terminal and intercalary). | Acid, gas. | Acid, gas. | Acid, late gas. | — |
| R.B.M. .. | Creamy colonies. Yeasty smell. | No surface growth. | Medium sized greyish colonies. | Branched mycelium and chlamydospores (terminal and intercalary). | Acid, gas. | Acid, gas. | Acid. | — |
| M.G. .. | Creamy colonies. Yeasty smell. | No surface growth. | Medium sized greyish colonies. | Branched mycelium and chlamydospores (terminal and intercalary). | Acid, gas. | Acid, gas. | Acid, gas. | — |
| M.G.D. .. | Creamy colonies. Yeasty smell. | No surface growth. | Medium sized greyish colonies. | Branched mycelium and chlamydospores (terminal and intercalary). | Acid, gas. | Acid, gas. | Acid, gas. | — |

route. (In the first case no veins were examined, and in the last sections were prepared of only one which showed thrombosis and organization.)

In each of the four cases 5% glucose solution was used as part of the intravenous therapy, and although the organism isolated from Case II (this experiment was not performed with the organism isolated from the other three cases) grew readily in a bottle of 5% glucose solution, it cannot be denied that thrombosis of the vein *plus* subsequent growth of the fungus in the clot as a result of the monilæmia may have occurred. It should be noted here that in 22 out of the 26 cases reported by Lederer and McLaren Todd intravenous therapy was required, but it is not stated whether in their two cases of monilæmia intravenous therapy was given.

It was not possible to trace the bottles of glucose and saline solution given to these patients in our series. However, several random bottles were sterile, and attempts at culture from the drip apparatus were unsuccessful.

All intravenous infusions carry a risk of pyæmia, especially when the open method is used (as was the case at the Brisbane Children's Hospital at the time of occurrence of these cases). Dodd and Rapoport draw attention to this and report one case of septicæmia (possibly from *Aerobacter aerogenes*) in which the organism was recovered from the blood-stream, the site of needle puncture and the bottle of hydrolysate used.

### Conclusions and Summary.

Monilæmia with mycotic abscesses in the viscera forms a pathological entity.

Four cases occurring in infants of low vitality suffering from enterocolitis are described. All four had intravenous therapy with 5% glucose solution. Oral and œsophageal thrush was present in one case only.

The source of infection in these four cases—whether from the pharynx or via the intravenous route—was not proved, but the latter was strongly suggested.

The diagnosis depends on the awareness of the occurrence of the infection, on the cultural and microscopic findings, and especially on the use of Gram's stain for suspected lesions.

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### Legends to Illustrations.

FIGURE I.—Mycotic abscess in kidney.

FIGURE II.—Mycelia and spores of Monilia in kidney abscess (Gram's stain).

FIGURE III.—Mycotic abscesses in myocardium. Note central necrosis and peripheral exudate.

FIGURE IV.—Mycelia, blastospores and chlamydospores in mycotic abscess of myocardium.

FIGURE V.—Thrombus in vein over medial malleolus.

FIGURE VI.—Fragment of mycelium near edge of thrombus of vein of ankle.

## EFFECT OF MINUTE PRELIMINARY DOSES OF METHYLCHOLANTHRENE UPON SUBSEQUENT CARCINOGENIC DOSES IN MICE.


By C. P. O'FLYNN,

*From the Institute of Medical Research, The Royal North Shore Hospital of Sydney.*


DURING the course of an experiment in which methylcholanthrene was being used to induce sarcoma in male mice, it was noticed that after six months one group of animals had failed to grow tumours at the site of injection. Examination of the records showed that instead of receiving 0·004 gramme these mice had been given only 0·0004 gramme in 0·1 millilitre of peanut oil, owing to a miscalculation.

### Experimental Account.

These animals were then given, at another site, 0·004 gramme of methylcholanthrene in 0·1 millilitre of peanut oil. After a further three months only one animal had grown a tumour, and that was at the site of the original injection. The remainder showed the following effects.

1. At the original site, either no abnormality or small reactive nodules of fibrous and areolar tissue.

2. At the site of the second injection, abscesses with sarcomatous walls in three cases, abscess with fibrous walls in one case, no abnormality in one case. From two of the abscesses was recovered a small quantity of peanut oil containing crystals resembling methylcholanthrene.

### Procedure in Controlled Experiment.

It was decided to repeat the experiment with a larger number of younger mice and adequate controls.

#### *Material.*

Male white mice at the age of sixty days were used. In previous experiments this strain had been observed to have the following characteristics: (i) an incidence of spontaneous mammary cancer less than 1:1000; (ii) a high susceptibility to the carcinogenic action of methylcholanthrene (80% to 90% grew tumours within five months of subcutaneous administration of 0·004 gramme of methylcholanthrene in peanut oil).

Methylcholanthrene dissolved in peanut oil was the carcinogen employed in this experiment.

#### *Method.*

Thirty mice were each given a subcutaneous injection of 0·004 gramme of methylcholanthrene in 0·1 millilitre of peanut oil in the sacral region (site I). Control mice were given no injection. After six weeks all the animals received 0·004 gramme of methylcholanthrene subcutaneously in the abdominal wall (site II).

ILLUSTRATIONS TO THE ARTICLE BY DR. J. V. DUHIG AND DR. MARGARET MEAD.

FIGURE I.

FIGURE II.

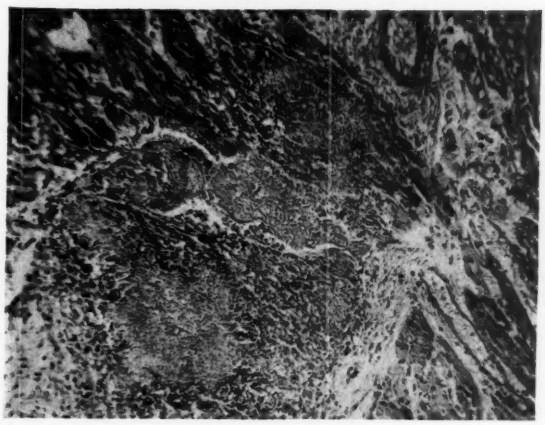

FIGURE III.

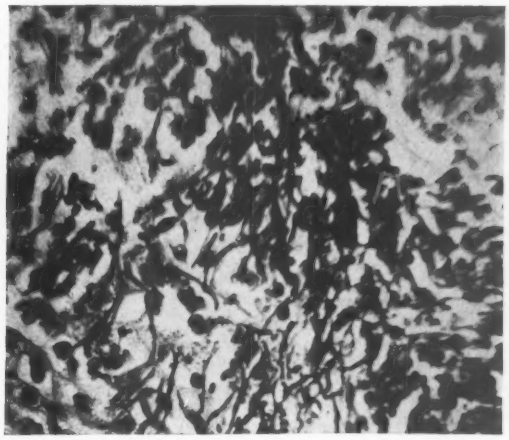

FIGURE IV.

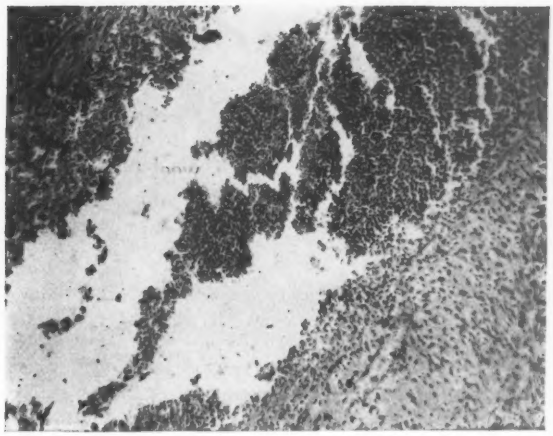

FIGURE V.

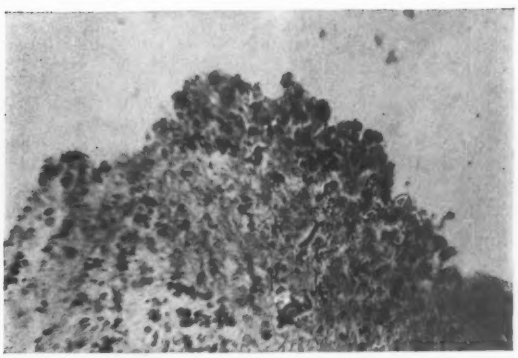

FIGURE VI.

## ILLUSTRATIONS TO THE ARTICLE BY DR. C. P. O'FLYNN.

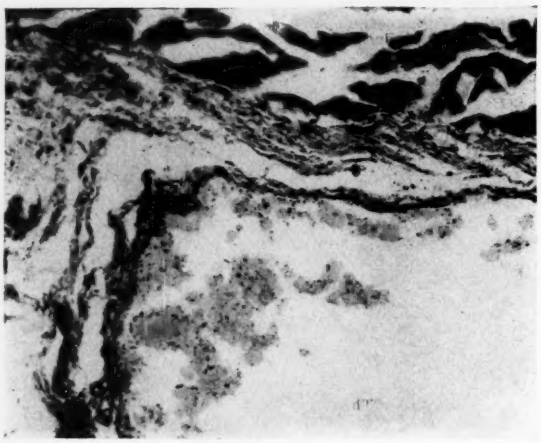

FIGURE II.

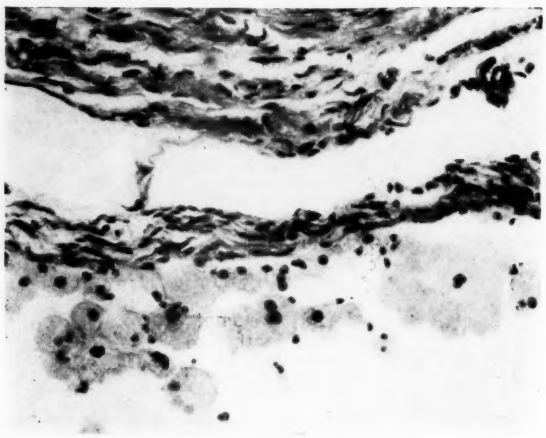

FIGURE IIA.

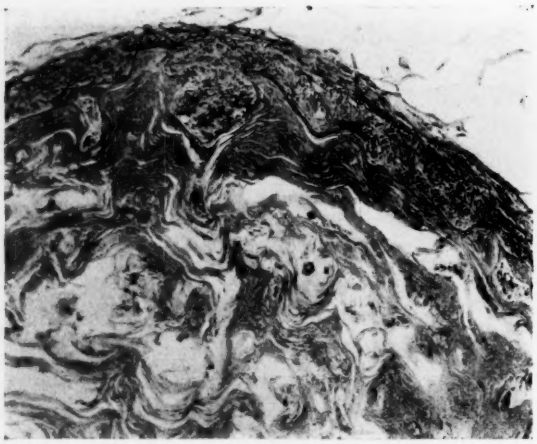

FIGURE III.

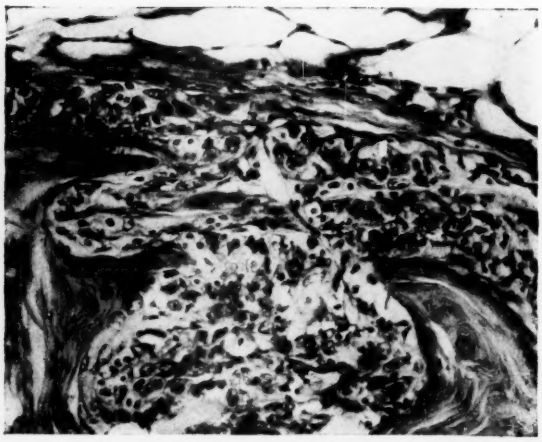

FIGURE IIIA.

FIGURE IV.

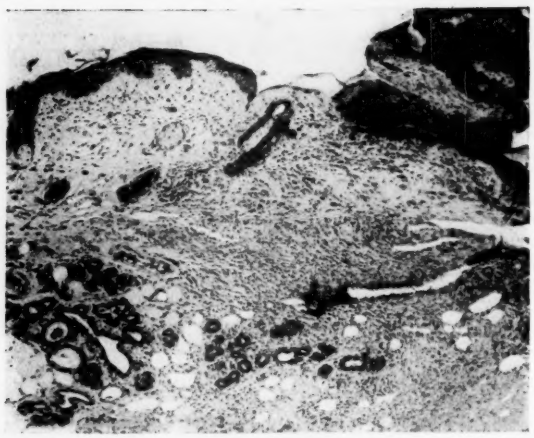

FIGURE V.

*Measurement of Resulting Lesions.*

Weighing of neoplastic masses was at first considered, but was not carried out, (*a*) because of the difficulty of defining the limits of infiltrating abscess walls, and (*b*) because it was desired to preserve portions of some of the lesions *in situ* for demonstration.

Two methods of measurement were used: (i) estimation of volume of tumour mass (and abscess cavities) by means of formula $4/3\pi abc$, where $a$, $b$ and $c$ are radii of an ellipsoid; (ii) estimation of mean linear diameters (Mayneord, 1932; Schrek, 1935).

The first of these methods was considered to be more accurate and the results have been shown accordingly; there was a slight source of error in the mean diameter method by reason of the fact that many of the tumours invaded deeply, but a comparison of the average mean diameter with the average estimated volume in this series showed this method in a very favourable light.

## General Results.

Tumours began to appear in the mice within fifty days. When these had reached a mean diameter of about 20 millimetres the animal was killed and an animal from the other group was killed at the same time. This was done also when any mouse died. At the end of 196 days all remaining mice were killed and examined.

Of the 30 "experimental" mice, seven had lesions at site I at the time of death. Three of these were malignant (number 5 (122 days) had a small multiloculated abscess with malignant change in the walls; number 19 (170 days) and number 24 (190) had spindle-cell sarcomata). At site II, 27 lesions were found. These had considerable histological variation. Twenty were neoplastic, but of these only 13 were uncomplicated sarcomata. The others all contained epithelial elements, in various stages of malignancy. (In one case the tumour was a well-encapsulated adenoma.) Six were abscesses with no malignant change in the walls, and contained either pus or keratin plugs; two were small fibromata.

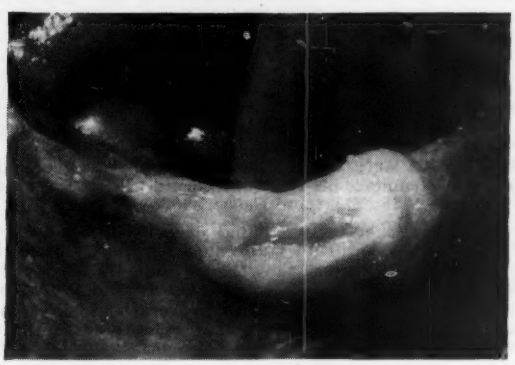

FIGURE I.

Lesion on abdominal wall of mouse one hundred and twenty-five days after second injection. (× 5.)

In the control animals, 25 of the lesions were sarcomata; one animal had a small area of squamous carcinoma, one a fibroma and three no abnormality.

## Post-Mortem Appearances.

*Site I.*

Two mice grew spindle-cell sarcomata, one of which (number 19) completely surrounded the butt of the tail, but did not invade bone. One animal had a small multiloculated abscess, the walls of which were sarcomatous.

In the remaining cases in which anything of note was found *post mortem*, it took the form of a mass of areolar and fibrous tissue, in which no malignant features could be seen.

*Site II.*

*Sarcomata*: Sarcomata were for the most part firm, fleshy tumours (in some cases with necrotic and hæmorrhagic centres), which were adherent to underlying muscle but not to skin, except in a few cases. One, which had invaded skin widely and deeply, was found to be a rhabdomyosarcoma.

*Abscesses and Cysts*: Some of the animals developed abscesses or cysts at site II. In two cases a small quantity of oil containing yellow crystals, presumed to be methylcholanthrene, was recovered when these were opened.

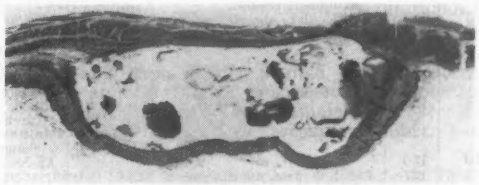

FIGURE IA.

Cross section of lesion in Figure I. (× 5.)

(Number 6 (125 days after injection) and number 13 (144 days after injection) (Figures I and IA).

*Changes in Other Organs*: No malignant change was seen in other organs *post mortem*.

*Histological Appearances.*

*Sarcomata*: The sarcomata were nearly all of spindle-cell type, but in some there were slight variations from place to place, and parts of these tumours looked as if they might contain myogenic elements. One was a frank rhabdomyosarcoma. These tumours resembled those described by Haddow (1939) in that they tended to invade muscle, but not skin or bone, and in no case did they form metastases in distant organs. They became necrotic in the centre fairly readily.

*Sarcoma and Squamous Carcinoma*: There was a mixture of spindle-cell sarcoma and squamous carcinoma in one case. No connexion could be traced between the malignant epithelial cells, which lay deep to the collagenous layer of the dermis, and the squamous epithelium of the epidermis, which showed no malignant change. In the other specimen the squamous epithelium was very much less malignant, but "cell nests" were found deep in the spindle-cell sarcoma, which was subcutaneous. Again the overlying skin was not malignant.

*Sarcoma and Mammary Hyperplasia in a Male Mouse*: One specimen has an ulcer with a sarcomatous floor one to two millimetres thick. The adjoining squamous epithelium covering the nipple is hyperplastic, and "cell nests" can be seen in the subjacent dermis. The mammary tissue is grossly hyperplastic and resembles that of a female animal (Figure V).

*Abscesses with Sarcomatous Walls*: Abscess with sarcomatous walls varied from those in which fibrous tissue walls were undergoing malignant change to those with walls composed entirely of spindle-cell sarcoma. They contained blood, polymorphonuclear cells and histiocytes.

*Abscesses with Carcinomatous Walls*: Abscesses with carcinomatous walls varied from those with fibrous tissue walls to those with sarcomatous walls, lined with squamous epithelium undergoing hydropic degeneration and early malignant change. They contained keratin, blood, histiocytes, polymorphonuclear cells, and epithelial *débris*. A notable feature was the presence of large numbers of cells of the *stratum granulosum* which were larger and contained more eleidin than is commonly seen in the granulosum layer of the skin in this strain of mice (Figures III, IIIA and IV).

*No Malignant Change*: Specimens with no malignant change were abscesses containing blood, polymorphonuclear cells and histiocytes, with benign and in some cases very well-formed fibrous tissue walls, which were unlined; or

TABLE I.

| Number. | Days. | Experimental. Lesion at Site I. | Estimated Volume. (Cubic Millimetres.) | Experimental. Lesion at Site II. | Estimated Volume. (Cubic Millimetres.) | Control. Lesion. | Estimated Volume. (Cubic Millimetres.) |
|---|---|---|---|---|---|---|---|
| 1 | 50 | | | Ulcer. Floor spindle-cell sarcoma. | 100 | Spindle-cell sarcoma. | 250 |
| 2 | 75 | | | Abscess. Wall sarcomatous. | 112 | Spindle-cell sarcoma. | 200 |
| 3 | 108 | | | Abscess. Wall early sarcoma. | 100 | Rhabdosarcoma. | 784 |
| 4 | 120 | Areolar. Reactive mass. No malignant change. | | Abscess. Wall early sarcoma. | 50 | ? Rhabdosarcoma. | 400 |
| 5 | 122 | Multilocular abscess, malignant walls. | | Abscess and spindle-cell sarcoma. | 128 | Spindle-cell sarcoma. | 560 |
| 6 | 125 | | | Cyst containing keratin and pus. No malignant change. | | Spindle-cell sarcoma. | 500 |
| 7 | 125 | | | Cyst lined with squamous epithelium. | | ? Rhabdosarcoma. | 240 |
| 8 | 125 | | | Mixed sarcoma and squamous carcinoma. | 80 | Spindle-cell sarcoma. | 134 |
| 9 | 125 | | | Multilocated cyst. No malignant change. | | Diffuse invasion of muscle spindle cells. | |
| 10 | 130 | | | Abscess. Sarcomatous walls. | 72 | Spindle-cell sarcoma. | 250 |
| 11 | 137 | Reactive mass, not malignant. | | Cyst-lined squamous epithelium containing keratin. | | Mixed-cell sarcoma, very pleomorphic. | 840 |
| 12 | 144 | | | Reactive and areolar mass, not malignant. | | Large abscess, malignant walls. | 250 |
| 13 | 144 | | | Cyst, very thin fibrous wall, not malignant. | | Spindle-cell sarcoma. | 980 |
| 14 | 144 | | | Spindle-cell sarcoma. | 896 | Spindle-cell sarcoma. | 172 |
| 15 | 155 | | | Abscess. Wall sarcoma lining squamous epithelium. | 54 | Spindle-cell sarcoma. | 288 |
| 16 | 155 | | | Ulcer. Sarcoma floor. Glandular and epithelial hyperplasia. | 72 | Mixed-cell sarcoma. | 168 |
| 17 | 155 | | | Spindle-cell sarcoma. | 146 | Fibrous nodule. ? Early malignant change. | |
| 18 | 165 | | | Fibrous nodule. ? Early sarcomatous degeneration. | | Spindle-cell sarcoma. | 200 |
| 19 | 170 | Spindle-cell sarcoma. | 192 | Spindle-cell sarcoma. | 672 | Spindle-cell sarcoma (very necrotic). | 840 |
| 20 | 185 | | | Œdematous necrotic mass, not malignant. | | Spindle-cell sarcoma. | 72 |
| 21 | 185 | | | Spindle-cell sarcoma. | 36 | Spindle-cell sarcoma. | 360 |
| 22 | 185 | | | Rhabdosarcoma (doubtful). | 240 | ? Rhabdosarcoma. | 720 |
| 23 | 190 | Spindle-cell sarcoma. | 896 | No abnormality found. | | Reactive tissue, not malignant. | |
| 24 | 190 | | | Spindle-cell sarcoma. | 670 | Spindle-cell sarcoma. | 250 |
| 25 | 190 | Reactive and areolar tissue. | | Mixed cell sarcoma. | 256 | Spindle-cell sarcoma. | 288 |
| 26 | 196 | | | Abscess. No malignant change. | | Spindle-cell sarcoma. | 120 |
| 27 | 196 | Small fibrous nodule. | | Adenoma. | | Spindle-cell sarcoma. | 240 |
| 28 | 196 | | | Spindle-cell sarcoma. | 160 | No abnormality. | |
| 29 | 196 | | | No abnormality. | | No abnormality. | |
| 30 | 196 | | | No abnormality. | | No abnormality. | |

else they were lined with benign but often irregular stratified squamous epithelium and contained keratin and epithelial *débris*.

*Cysts*: The cysts were simple cysts with fibrous tissue walls in which no malignant change could be seen. From two of these a small quantity of oil containing yellow crystals was recovered. Microscopically they were seen to contain cells resembling histiocytes, in the cytoplasm of which was some lipoid material, possibly peanut oil (Figures II and IIA).

*Fibroma*: In one animal there was a small fibrous nodule in the dermis; it was undergoing early myxomatous degeneration.

*Adenoma*: One animal grew an adenoma, the appearance of which suggested that it might be derived from either sweat gland or mammary tissue. It was well encapsulated.

## Historical Account.

### *Chemical Carcinogenesis.*

In 1775 cancer of the scrotum in chimney sweeps was first described by Percival Pott. This was the first time that "occupational" cancer was recognized and correctly attributed to the carcinogenic agents present in soot. After this many other "occupational" cancers were described among workers whose work exposed them to prolonged contact with pitch, soot, creosote and tar.

This naturally was followed by attempts to produce cancer in experimental animals, by means of tar, creosote *et cetera*. Hanau (1889) painted rats with tar, but obtained only chronic dermatitis; Bayon (1912) produced a non-invasive papilloma by injection of coal tar into the ear of a rabbit; Yamagiwa and Ichikawa (1915) produced papillomata and carcinomata by painting rabbits' ears with tar over a long period. This was followed by a spate of work on the subject, as a result of which it was observed that mice and rabbits were susceptible to the carcinogenic action of tar on the skin; rats', dogs', guinea-pigs' and fowls' skins were not susceptible. However, subcutaneous injections of tar produced sarcomata in these animals (Woglom, 1926; Selig and Cooper, 1933).

In 1930 Hieger observed that carcinogenic tars all had a fluorescence spectrum with characteristic bands at 4000, 4180, and 4400 Å., and these bands were like those of the fluorescence spectrum of 1:2:benzanthracene. Kennaway (1930) made a special study of hydrocarbons allied to 1:2 dibenzanthrene and found that 1:2:5:6 dibenzanthracene was carcinogenic.

Further researches by other workers have produced large numbers of carcinogenic hydrocarbons, the most powerful of which are 9:10 dimethyl 1:2 benzanthracene, and methylcholanthrene.

## Mode of Action of Carcinogenic Hydrocarbons in the Tissues.

### *Tissue Culture.*

Hearne (1936) found that when mouse fibroblasts were grown in a culture medium containing methylcholanthrene, after three days the culture contained a high percentage of abnormal mitotic figures and chromosome pairing, and chiasma formation had been induced.

M. R. Lewis (1935) found that in chick embryo cultures to which carcinogenic hydrocarbons had been added, the cells acquired photosensitivity, and that this was often accompanied by inhibition of cell division and mitotic aberrations resembling many of the types seen in malignant

growths. But W. H. Lewis (1935) prefers the theory that the changes are cytoplasmic or somatic rather than chromosomatic. And Willis (1947) states that "no worker has yet proved the induction of neoplastic change in tissue cultures treated by carcinogens".

*Epithelium.*

Page (1938) observed that cholanthrene and methylcholanthrene had an early and definite effect on the cell structures—a toxic effect, shown by the death of cells; an attempt at protection, shown by an increase in the amount of cornified material laid down at the site of repeated applications, an immediate increase in the size of the nucleoli of epithelial cells (twice to two and a half times

TABLE II.

| Finding. | Experimental Mice. | Controls. | Total. |
|---|---|---|---|
| Malignant change .. | 19 | 26 | 45 |
| No malignant change .. | 11 | 4 | 15 |
| Totals .. .. | 30 | 30 | 60 |

$\chi^2 = 4{\cdot}356$ for one degree of freedom. $P<0{\cdot}05$.

normal in one week) and a further increase in size when a malignant lesion occurred. He found no evidence that inflammatory reaction played any part in carcinogenesis, but attributed the carcinogenic effect to direct stimulation of the nucleus and nucleolus.

Cowdry and Paletta (1941) found a progressive increase in the nuclear and cytoplasmic volumes of basal and spinous cells, with increased mitosis, especially in basal cells. They also noticed a great diminution in nuclear viscosity in malignant cells, which they suggested might be related to changes in mineral and water content.

Guttman and Halpern (1935) state that the volume of nucleoli of normal tissue is "significantly smaller than the volume of nucleoli of hyperplastic tissue, and of benign and malignant tumours. There is no significant difference between the nucleolar volume of benign tumours and malignant tumours".

*Connective Tissue.*

Orr (1939) found that implantation of pellets containing a carcinogen was followed by the development at the site of an incompetent "foreign body reaction", that the reactive tissue was poor in quality and quantity, and that encapsulation did not occur. The development of sarcomata near the site of reaction seemed to be related to incomplete tissue response caused by the carcinogen.

*Chemical Changes.*

Methylcholanthrene is closely related chemically to the bile acids and has been prepared from deoxycholic acid and cholic acid; "the changes by which it is obtained from deoxycholic acid are all reactions of the type which are known to occur normally in the animal body, although there is no evidence that this particular sequence of changes . . . does actually occur in nature" (Barry *et alii*, 1935).

Fieser (1938) concludes that hydrocarbon undergoes rapid alteration in the animal body, that most of it is exhausted before tumours begin to appear, and that this reaction is "the first step in a time-consuming and complicated chain of events leading eventually to malignant growth".

### Acquired Resistance to Transplanted Tumours.

Acquired resistance to transplanted tumours was extensively investigated by Bashford, Murray, Haaland, Bowen and Russell between 1908 and 1912.

Russell (1912) found that different tumour strains differed widely in their powers of inducing resistance to reinoculation. Extreme variations of behaviour occurred. One strain of tumour grew progressively in almost all inoculated mice, and its growth afforded no protection to subsequent inoculation with the same strain of tumour. Another strain of tumour grew temporarily and then regressed in nearly every case. Growth of this tumour induced in nearly every mouse a refractory state to subsequent inoculation with the previously mentioned strain.

Foulds (1930), using the same two strains, obtained similar results, but found in addition that substrains of the same growth might vary in their powers of inducing resistance; he furthermore suggests that with homologous transplants which do not confer immunity the tumour cells have lost their susceptibility to the resistance which they induce.

Mottram and Russ (1917) pointed out that decreasing growth rate in "curvilinear progressive" and "curvilinear non-progressive" tumours (for example, R.39 sarcoma and Brown-Pearce carcinoma) was "presumably due to acquired immunity of the animal host".

Andervont (1932) concluded that variations in immunity were influenced by (i) the inherent property of the tumour, (ii) variations in growth energy, and (iii) differences in animals inoculated.

Domagk and Hackmann (1935) succeeded in preparing labile cell-free extracts from tumours, which, in three or four small doses given beforehand at intervals of a few days, are said to have produced a refractory state which inhibited the growth of transplants. Large doses, however, stimulated the growth of established neoplasms.

On the other hand, Bittner (1936) found that concomitant immunity was non-specific and that it varied with different strains of animals; in addition, no concomitant immunity was produced to tumours which arose spontaneously in pure stock after caudal inoculation with tumour 180 or homologous tissue.

### Sensitization of Tissue to Action of Carcinogenic Hydrocarbons.

Simpson and Cramer (1945) discovered that methylcholanthrene dissolved in anhydrous lanolin was rendered inactive carcinogenically. That this inactivity was not due to lack of absorption was demonstrated by the fluorescent spectra of skins of treated animals.

Subsequent treatment of these animals with methylcholanthrene in the "active state", by painting with a solution of benzene, showed in a large series of mice that carcinoma of skin was more readily induced than in untreated controls.

### Inhibition of Tumour Growth by Carcinogenic Hydrocarbons.

Haddow (1947) found that parenteral injection of carcinogenic hydrocarbons in mice having spontaneous neoplasm (mainly carcinoma of mammary glands) "resulted in most cases in prolonged inhibition in the rate of tumour growth", and, having experimented in the same way on sarcomata induced in mice, he found that "primary chemically induced sarcomata as a class tend to be considerably less susceptible to the inhibitory action of carcinogenic substances than spontaneous or transplanted tumours". He states that "this relative resistance is not, however, specific, since tumours induced by a given carcinogenic compound were not significantly more resistant to the inhibitory action of the same compound than that of other carcinogenic substances". He believed this inhibitory action to be due to toxicity of a special and possibly specific kind, rather than to general toxicity affecting the metabolism of the animal.

Pybus and Miller (1937) obtained similar results in mice bearing spontaneous mammary tumours, but found that formation of new tumours was not prevented. They also found that this form of treatment (intraperitoneal injection) had no effect on sarcomata or leuchæmia. Histologically they described an increase in scirrhous and

fibrosed types of tumour, and the connective tissue elements were well developed in many of the tumours.

Stamer (1943), in several series of carefully controlled experiments, found: (i) that carcinogenic hydrocarbons could cure transplanted leuchæmia in mice; (ii) that carcinogenic hydrocarbons had no specific effect on induced, spontaneous or transplanted tumours, and showed clearly that any apparent inhibition was due entirely to the general toxic effect on the animal; and (iii) that the toxic effect of the drug was much greater when it was dissolved in olive oil than when it was suspended in water.

## Discussion.

In the series of experiments described several points seem worthy of further investigation. On the figures it would seem that some degree of inhibition of the carcinogenic effect of the hydrocarbon used was obtained by previous administration of a "desensitizing" dose in quantities which, for want of a better word, may be called homœopathic.

Now let us compare the results obtained by Pybus and Miller (1937), Haddow (1938) and Stamer (1943).

Pybus and Miller, and Haddow agree that the administration by parenteral injection of a carcinogenic hydrocarbon has an inhibitory effect upon spontaneous mammary tumours in mice but not upon sarcomata. Haddow states that his sarcomata were induced. The other workers do not mention whether the growths were induced or transplanted. They attributed the inhibitory effect of the hydrocarbon to a property of a "special, but not a specific" kind. Stamer, on the other hand, seems to have shown, past reasonable doubt, that the inhibitory effect was due to a general toxic effect on the animals' metabolism. Is it then a reasonable inference to draw that the original "tumour-producing" dose of carcinogen (in Haddow's series) may have had a "desensitizing" effect upon the animal as a whole, which rendered it refractory to the toxic effect of the subsequent intraperitoneal "therapeutic" doses?

Against this may be set the fact that in several series of rats and mice multiple tumours have been produced by subcutaneous administration of hydrocarbon into one to four loci in mice and into one to twelve loci in rats. But this is only an apparent contradiction, as the injections in these cases were given simultaneously, so far as can be gathered from the report of the work (Dunning, Curtis and Bullock, 1936).

Again, tumours have been produced in rats by repeated subcutaneous injections, at weekly intervals, of methylcholanthrene in lard. But as the dose in the first injection (two or three milligrammes in one millilitre) would have been enough to produce a tumour in any case, I think that this too is only an apparent contradiction (Barry, Cook, Haslewood *et alii*, 1935).

Another feature worthy of interest is the appearance in the "experimental" mice of proliferation of epithelial elements, in three cases to the point of malignant change. These may be epithelial cells carried in at the time of injection of the carcinogen and subsequently acted on in the deep tissues by the carcinogen. In no case could a connexion between these growths and the squamous epithelium of the overlying skin be traced, and in no case was the skin undergoing malignant change. This phenomenon was not seen in any of the "control" series. If these are the result of epithelial implantation, they must have arisen from a very small number of cells, as the needle used was of very small bore.

Smith (1950) describes a metaplasia of epithelial cells of embryo lung alveoli (introduced, with methylcholanthrene, into the muscle of mouse thigh) which resulted in squamous epithelium. He also succeeded in producing "indubitable carcinomas" from such implants. He does not mention whether the introduced methylcholanthrene produced any sarcomatous change in the tissues of the host.

At first sight this would seem to lead to the conclusion that in some cases the carcinogen exercised some sort of selective action on the implants, as in nine cases they have grown and in three cases become malignant, whilst the surrounding connective tissue has shown either no malignant change or very little.

But Dunning, Curtis and Bullock (1936) point out that "potency for malignancy must be a universal cell characteristic and that histogenesis of these [induced] tumours was determined by the fortuitous exposure to the irritant of the various types of cells". And Simpson and Cramer (1945) succeeded in sensitizing mouse epithelium to the carcinogenic effect of methylcholanthrene by previous exposure to the carcinogen in an inactive form.

Is there then, in the present series, evidence of either a "sensitization" of epithelial elements or a "desensitization" of connective tissue elements, by the administration of minimal preliminary doses? This, in view of the fact that methylcholanthrene given subcutaneously is far more likely to produce a spindle-cell sarcoma of a type described as follows by Barry *et alii* (1936); it has, they state, "on the whole a more fibromatous appearance than those produced by other hydrocarbons. Numerous giant cells are present in some of them. The invasive power of these tumours appears to be rather low in spite of their great size . . . ."This was the appearance of most of the tumours of the series here discussed. (However, in a previous experiment I have succeeded in producing adenocarcinomata in the breasts of pregnant mice with methylcholanthrene.)

The figures given by Dunning, Curtis and Bullock (1936) show that with the use of benzpyrene in 452 mice the types of tumour induced were as follows: sarcomata, myogenic or probably myogenic (63%) *plus* spindle, mixed cell or fibrosarcoma (37%), 427 (94·4%); adenocarcinoma and sarcoma, two (0·44%); squamous epithelioma and sarcoma, 23 (5·09%).

Rask-Nielsen (1948), having injected 9.10 dimethyl 1.2 benzanthracene into various animal tissues, concluded that the hydrocarbon was "capable of inducing specific tumors only in spontaneously tumor-producing tissues". He found that "direct carcinogenic action induced development of local specific tumors in certain spontaneously tumor-producing organs (thymus, lung, subcutaneous tissue) but not in the remaining spontaneously tumor-producing organs (lymph node, spleen, mammary tissue and skin)", and "not spontaneously tumor-producing organs (kidney and testis) exhibited one case of local specific tumor-formation (a testicular carcinoma) but no tumor following application to other organs".

Differences in strains of mice also have some bearing upon the type of response evoked. Esmarch (1940), using Bagg albino mice, a strain which seldom develops spontaneous tumours, induced 38 tumours with eight to ten milligrammes of methylcholanthrene. Of these only two were spindle-cell sarcomata. The others were mixtures of squamous carcinoma and spindle-cell sarcoma.

However, I find that in the strain of mice used in this experiment the usual response to subcutaneous administration of methylcholanthrene is a spindle-cell sarcoma, unmixed with other types of neoplasm. The literature on the subject teems with further instances of variations in response between different strains of mice to the same carcinogen, and such response appears consistently in these strains. In addition, there are examples of differences in response in the same strain to different carcinogenic hydrocarbons, and it has been shown by Simpson and Cramer that it is possible to sensitize a tissue to the effect of a carcinogen. It must also be borne in mind that the epithelia of rats, guinea-pigs and fowls are not susceptible to the carcinogenic action of hydrocarbons.

In the present experiment a preliminary minute dose appears to have upset the usual response in the strain of mice used, in that the production of sarcomatous tissue was to some degree inhibited and the epithelial elements tended to proliferate. These observations surely seem to modify the view of Dunning, Cortis and Bullock that the histogenesis of the induced tumour is entirely fortuitous.

If the present results are compared with those of Haddow and of Pybus and Miller, and with the observations and theories of Mottram and Russ on the growth rates of curvilinear tumours, they may indicate that a protective response has been evoked in the connective-tissue elements by the administration of a minute preliminary dose. They seem to be incompatible with the results of Simpson and Cramer; but as their preliminary dose of carcinogen had been inactivated and was in fact not carcinogenic, it is felt that the experiments are not quite parallel.

Another striking feature was the variation in sensitivity in the same strain of mice to the effect of tiny doses, three mice in 30 showing a definite malignant response to 0·0004 gramme.

## Summary.

1. The result of a controlled experiment on a series of 30 male white mice is presented and the related literature is briefly reviewed.

2. In some of the animals the administration of a minute preliminary dose of methycholanthrene appeared to induce a refractory state in the tissues to subsequent "carcinogenic" doses.

3. In two cases some of the solution of methylcholanthrene was recovered from the site of injection after 125 and 144 days.

4. These results appear to conflict with those of Simpson and Cramer and of Stamer, but to be compatible with those of Mottram and Russ, of Pybus and Miller and of Haddow.

5. The opinion that the histogenesis of induced tumours is entirely fortuitous seems to the writer to require modification.

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## Legends to Illustrations.

FIGURE II.—Cyst with fibrous tissue wall, containing cells resembling histiocytes. No malignant change seen. (× 75.)

FIGURE IIA.—High-power view of Figure II. Lipoid material can be seen in cytoplasm of histiocyte-like cells. (× 300.)

FIGURE III.—Cyst containing keratin. Walls lined by very irregular squamous epithelium. (× 75.)

FIGURE IIIA.—High-power view of squamous cells in Figure III. (× 300.)

FIGURE IV.—Cyst with fibrous tissue walls, lined with stratified squamous epithelium, containing keratin, and showing exaggeration of *stratum granulosum*. (× 75.)

FIGURE V.—Breast of male mouse, showing ulceration in relation to hyperplastic nipple, sarcomatous change in dermis, and benign hyperplasia of mammary tissue, resembling lactating breast. (× 75.)

# THE CHANGING PLACE OF CÆSAREAN SECTION.[1]

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## Historical Survey.

THE most spectacular procedure in obstetrics is the delivery of the infant by abdominal incision into the uterus —Cæsarean section, the kingly cut, the *"Kaiserschnitt"* of the Germans, the surgical master stroke of the art. In no other operation in the realms of general surgery are two lives at stake. It has a remarkable history which has been the subject of many writings, notably by J. H. Young (1944). The changing place it has come to occupy in obstetrics over the years is an accurate reflection of the many spectacular advances in medicine. It was performed in times of antiquity as a funeral rite before burial, and legislated for by the Romans to be performed on the dead woman in an attempt to save the child. Prior to 1500, there is no evidence of a deliberate and successful operation upon a living woman. In that year, a desperate and distracted Swiss veterinary surgeon, so it is said, successfully performed a Cæsarean section on his own wife, who survived to bear him twins and three more children besides (Young, 1944).

> One day in the year A.D. 1500, the wife of a sow gelder, named Jacob Nufer, went into labour. For reasons not clear, she was quite unable to deliver herself of the child. Midwife after midwife was summoned until no fewer than thirteen had tried to help the unfortunate woman, but without result. Then to the astonishment of the neighbours, the husband sent for the local lithotomists, but however skilful these gentlemen may have been in their chosen profession, they were of no assistance in the crisis and the child remained unborn. Not unnaturally the husband was now desperate and he asked permission from the local Mayor to perform Cæsarean section. This was at first refused, but was granted on a second application. Imploring Divine aid, Jacob Nufer, using a razor, proceeded to perform a successful Cæsarean section. The patient made a good recovery and in later years gave birth to five other children, including one set of twins, by the natural route. The child which had made such a sensational start in life, lived to the age of seventy-seven.

The Italian, Porro, in 1876 eventrated the uterus and excised it over a snare, leaving the cervical stump in the wound. Six years later, in Germany, Sanger sutured the uterus in layers with buried suture material and brought the mortality rate into the respectable region of 50%. These, of course, were the times when the customary prelude to undergoing laparotomy was the execution of the last will and testament. Osiander (1759-1822), in his treatise, wrote as follows (Marshall, 1939):

> It cannot be denied that of the women who undergo Cæsarean section more than two-thirds die, and barely a third are saved. Cæsarean section belongs to those operations of which the outcome is entirely uncertain. Before, then, undertaking this procedure, one should allow the patient to draw up her will and grant her time to prepare herself for death.

Events moved rapidly with anæsthesia, Lister, and then asepsis. There now developed a serious rival to all those complicated vaginal manipulative procedures of the obstetrical art, the dexterous internal version, strenuous "high forceps", pubiotomy, perforation, crushings and other difficult *morcellements*. A new and alternative birth canal was opened up through the abdomen. To reduce the hazards of peritoneal soiling, man's ingenuity then sought alternative anatomical approaches—to the lower segment, transperitoneally over the bladder or extraperitoneally through the cave of Retzius.

However, all this belongs to history and these are a few *staccato* facts. To see it all it is necessary to stand apart and view in broad kaleidoscopic perspective the changing pages of the text-books of the previous generations; to see the gradual replacement of operative vaginal deliveries as increasing safety widened the indications for abdominal delivery. I have never seen a pubiotomy performed, nor are there records of one at the Women's Hospital, Melbourne. Greenhill records the difficulties surrounding the last one he saw De Lee perform in America in 1922.

### *Contemporary Period.*

The personal experience of the operation of those present at this meeting extends over perhaps thirty years. Speaking within the ambit of my own personal experience, let me quote to you the position twenty years ago, as expressed by my first teacher, Arthur Wilson, in his notes to us as students:

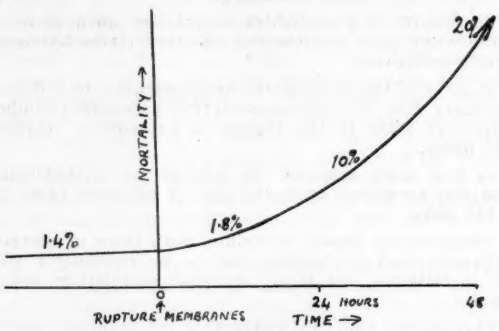


FIGURE I.
The mortality rate from Cæsarean section twenty years ago.

> For each hour the operation is delayed after rupture of the membranes, the mortality is increased by 1 per cent., each vaginal examination increases it by 1 per cent., attempts at forceps or other methods of delivery by 10-15 per cent., and the presence of an offensive vaginal discharge by 20 per cent.

And again let me quote mortality figures from Professor Marshall Allan's printed notes to the medical students: before labour, 1·4%; early in labour, 1·8%; late in labour, 10%; after induction, 14%; after "failed forceps", 25%; after attempted craniotomy, 50%. The figures he gives are based on Kerr and Holland's survey over a number of British hospitals, which is quoted in "Recent Advances in Obstetrics and Gynæcology" as late as 1939. These figures were for cases of disproportion in which the classical operation was performed, and they may be taken as reflecting the position twenty years ago. Without any pretence at accuracy, and purely diagrammatically, the position may be illustrated at that time as in Figure I.

## The Position Today.

From many parts of the world statistics are at hand to show that the mortality rate in premeditated cases is down to the level of the general operations of election in surgery, and in "clean" cases at least it is less than 1%. Over a twenty-year period—1924 to 1945 inclusive—there were 1134 Cæsarean sections at Queen Charlotte's Hospital with 36 deaths, a mortality rate of 3·2% ("Queen Charlotte's Text-Book of Obstetrics", 1948); but these include emergency cases and complicated cases from elsewhere, and they were dealt with before the penicillin era. A point of great importance with respect to operative mortality must be stressed. In gross figures the mortality rate is often that of the complicating abnormality. The death rate is, in fact, that of a collection of severe obstetrical emergencies in which one of the procedures of management happens to be a Cæsarean section. Corrected mortality figures are always viewed with circumspection; but there can be no doubt that the true mortality for the operation itself when performed on uninfected, healthy patients as a procedure of election is now very small. At the recent British Congress in London in 1949, Marshall and Cox (1949), as a result

[1] Read at a meeting of the Section of Obstetrics and Gynæcology, Australasian Medical Congress (British Medical Association), Seventh Session, Brisbane, May-June, 1950.

of a collective investigation over 19 British hospitals for the five recent years 1943 to 1947, record a gross maternal mortality rate of 0·99%, and an over-all incidence of Cæsarean section of 6·2%. Somewhat similar figures are recorded from America.

The diagram in Figure I was drawn to show the position about twenty years ago. As before, the position today may be represented very diagrammatically in Figure II. Now, if we superimpose Figure II over Figure I of perhaps twenty years ago, we pictorially (not accurately) represent the changes through which we have lived in our generation.

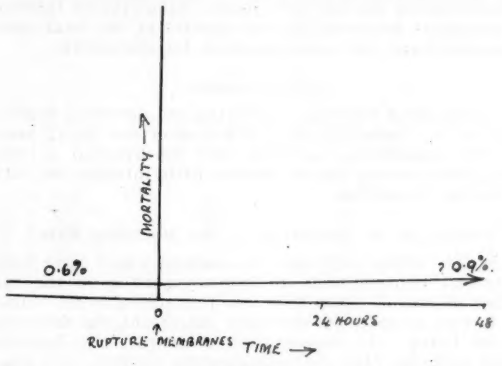


FIGURE II.

The mortality rate from Cæsarean section at the present time.

The outstanding feature is not so much the reduction in mortality in operations of election on uninfected patients, but in the pronounced flattening of the mortality curve from the time the membranes rupture. From the point of view of mortality, rupture of the membranes is a most important single incident in labour. It is the flattening of the mortality curve after this zero point has been reached

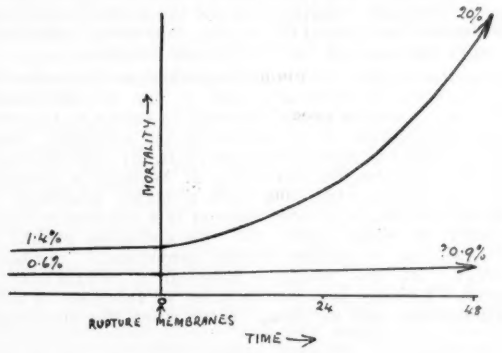


FIGURE III.

Figure II superimposed on Figure I, to show the changes that have occurred during a generation.

which has widened the field of usefulness of the operation and which has made possible the extended use of the trial of labour finesse in obstetrics by making progressive postponement of judgement relatively safe. It is this fact which is changing the face of the text-books in our own time. It has shifted attention away from the cold, mechanical factors in assessing the outcome of labour, to the observation of the summated physiological factors as labour progresses. It has made pubiotomy a nonentity in our own hospital statistics, and internal version, craniotomy and "high forceps" less frequent necessities, although it should be remembered that those factors which have made abdominal delivery safer have likewise made vaginal operative delivery also less risky. It has encouraged the best teaching hospitals in Great Britain to perform Cæsarean section on one in 16 of their patients (6·2%), and similarly the Americans. I cannot illustrate this better than by referring to figures quoted in the most recent Australian text-book of obstetrics by Bruce Mayes (1950). From figures quoted from the Royal Hospital for Women, Sydney, it is shown that the craniotomy rate there (excluding hydrocephalus) has been reduced from 5·19 per 1000 in the five years from 1926 to 1930 to 0·65 per 1000 in the period 1943 to 1947.

## Thirty-Year Review.

With the changing place of Cæsarean section in mind, the results over the last thirty years, ending June each year, were investigated from the records of the Women's Hospital, Melbourne.

TABLE I.

*Incidence and Mortality, 1919 to 1949.*

| Period of Five Years. | Deliveries. | Cæsarean Sections. | Incidence. | Maternal Deaths. | Mortality Rate. |
|---|---|---|---|---|---|
| 1919 to 1924 | 11,840 | 164 | 1·4% | 10 | 6·1% |
| 1925 to 1929 | 16,560 | 135 | 0·8% | 3 | 2·2% |
| 1930 to 1934 | 18,379 | 212 | 1·1% | 17 | 8·0% |
| 1935 to 1939 | 20,590 | 285 | 1·4% | 19 | 6·7% |
| 1940 to 1944 | 19,681 | 284 | 1·4% | 7 | 2·5% |
| 1945 to 1949 | 24,174 | 638 | 2·6% | 8 | 1·2% |
| 1919 to 1949 (thirty years) | 111,224 | 1718 | 1·5% | 64 | 3·7% |

The interval is divided into six periods of five years for convenience of perspective. Like the Queen Charlotte figures, the present figures cover all and sundry—such cases as come to a large maternity hospital—including Cæsarean hysterectomy, but not uterine rupture. It will be seen that there is some general correspondence of the over-all figures between the series of the two hospitals. The figures for the individual years of the last five-year period at the Women's Hospital, Melbourne, are as in Table II.

TABLE II.

*Mortality Rate, 1944 to 1949.*

| Year. | Deliveries. | Cæsarean Sections. | Maternal Deaths. | Mortality Rate. |
|---|---|---|---|---|
| 1944 to 1945 .. | 3853 | 89 | 1 | 1·1% |
| 1945 to 1946 .. | 4084 | 85 | 2 | 2·3% |
| 1946 to 1947 .. | 5477 | 176 | 3 | 1·7% |
| 1947 to 1948 .. | 5304 | 131 | 2 | 1·5% |
| 1948 to 1949 .. | 5456 | 157 | Nil | Nil |

The figures are so small that percentages are meaningless, although it may be noted that in the last statistical year in none of the 157 cases in which Cæsarean section was performed in the hospital did death occur. From Tables I and II the following factors are noteworthy:

1. The over-all mortality of the operation as performed for all cases shows a progressive decline in the Women's Hospital over the last twenty years. This decline is more pronounced in the last five years.

2. The scope of the operation, as reflected in the percentage incidence of the operation in relation to the total deliveries, is being extended so that in the last five-year period the operation was used nearly twice as frequently. This increased incidence commenced during the last three years. This incidence, by American standards, is still very low. D'Esopo (1950) reports an average incidence in 10 of the main eastern States hospitals as 4·9%, and he suggests that the optimum incidence should be between

5% and 6%. Douglas and Landesman (1950) quote an incidence of 3·3% in 245,000 deliveries over 20 leading clinics in the period from 1941 to 1945. The incidence of 6·2% over the best British hospitals, recorded by Marshall and Cox (1949), has already been mentioned. A factor in comparing figures may be variations in the ratio of hospital to home confinements.

It is reasonable to presume that the tendency to find this wider scope is encouraged by the diminished mortality. It is of course possible to reduce the mortality rate by the exercise of early decision and perhaps poor judgement, so that the operation is performed early in labour and at the least risky and the "cleanest" end of the scale. But it is likewise possible with increased safety to take into the statistical columns of Cæsarean section those risky cases in obstetrics which would otherwise be recorded under the headings of other manifestations. In this connexion it may be interesting to quote three cases, of which I have had personal experience, and which are included in the last year of this series in which there were no maternal deaths. It may well have been that the results were fortunate or that hysterectomy or extraperitoneal section would have shown better judgement in cases such as these.

CASE I.—A *primigravida*, aged thirty-one years, who had been married ten years and was anxious for a family, was admitted to hospital at the thirty-sixth week of pregnancy. There was little doubt the membranes had been ruptured for eight days, although contractions had been present for only twelve hours. The cord had prolapsed four and a half hours before her admission to hospital, but was pulsating slowly at a rate of 60 to 70 per minute. The cervix was dilated to admit two fingers, and the fœtus was presenting by the breech. A live baby weighing four pounds two ounces was delivered by Cæsarean section, and the puerperium was only mildly morbid.

CASE II.—A *primigravida*, aged twenty-five years, had been treated by stimulation for post-maturity. The membranes ruptured twenty-four hours before contractions commenced, and she had been in labour a further forty-six hours before her admission to hospital. The contractions were strong, the fundus was large and the fœtal heart was not heard. The thick, œdematous cervix was dilated to admit three fingers, the face was presenting with the chin posterior, and the head was entirely above the brim. Examination of vaginal smears revealed a coliform infection. Gastric aspiration, intravenous therapy and chemotherapy were employed, and at operation the peritoneal fluid had a thick yellow purulent appearance. The child, weighing nine pounds six ounces and post-mature, was stillborn. The puerperium was uneventful.

CASE III.—A patient, aged thirty-three years, with one child eleven years old, was admitted to hospital at thirty-six weeks with obstructed labour and the fœtus in a transverse presentation owing to a large myoma in the pelvis. Several attempts at delivery had already been made, and the prolapsed arm had been partly avulsed from a macerated fœtus. The cervical canal was reduced to a small crescentic slit, through which it was not possible to extract or morcellate the fœtus. At lower segment Cæsarean section two small myomata were removed from the line of the incision and the fœtus was extracted; but the large myoma buried deeply in the posterior part of the cervix was left *in situ* with the uterus. Convalescence was uninterrupted.

### *Cause of Maternal Deaths.*

The main cause of death over the series is set out in Table III.

Examination of the histories shows that a number of the deaths could not be attributed to the operation, as some patients were already seriously ill with one or other of the following conditions: generalized tuberculosis, nephritis, and liver toxæmia with vomiting and jaundice. One-third of the deaths resulted from infection, although none occurred during the last five years. Albuminuric toxæmia and eclampsia accounted for one-quarter of the total cases, and hæmorrhage and embolism each for one-eighth.

### *Fœtal Wastage.*

The total fœtal wastage (stillbirths and neo-natal deaths) is set out in Table IV; it is 15·4% over the thirty years with little significant variation over the five-year periods. These gross over-all figures provide little information without further dissection.

### *Factors in the Reduction of the Mortality Rate.*

It is interesting to dissect the factors which have made substantial contributions to improvement over the last number of years. Apart from the imponderable but important factors of obstetric skill and judgement, the following may be listed: (i) resuscitation measures, (ii) bacteriological methods, (iii) chemotherapeutic control, (iv) anæsthesia, (v) anticoagulants, (vi) gastric aspiration, (vii) operative technique.

*Resuscitation Measures.*—Blood transfusion and other forms of intravenous therapy, which were rare twenty or thirty years ago, are now commonplace in our obstetric hospitals. In ante-partum hæmorrhage they are particularly life-saving. Blood typing is a routine procedure in the ante-natal period, and every patient has her hæmoglobin value estimated twice so that deficiencies can be made good.

*Bacteriological Methods.*—A better appreciation of the sources from which infection arises, and its control by throat swabbing, masks and better antiseptics, have made their contribution. Assisting this are the improved methods of bacteriological technique in the laboratory, especially the rapid diagnosis of infectivity from smears.

*Chemotherapeutic Control.*—Chemotherapeutic control is of outstanding importance when it can be specifically applied to a sensitive organism which is shown by bacteriological examination to be present in the genitalia. Penicillin and sulphonamide drugs are so readily available and carry so few disadvantages that it becomes a question where we should stop. In such a major procedure as Cæsarean section, in which infection is a common cause of mortality, it would seem that the operation should be performed as a routine under prophylactic antibiotic coverage. At the Women's Hospital a compromise is adopted. Therapy is given in cases of infection or after manipulations, and in "clean" cases when the membranes

TABLE III.
*Cause of Death.*

| Main Cause. | 1919 to 1924. | 1925 to 1929. | 1930 to 1934. | 1935 to 1939. | 1940 to 1944. | 1945 to 1949. | Total. |
|---|---|---|---|---|---|---|---|
| Infection | 2 | 2 | 6 | 8 | 4 | Nil | 22 |
| Albuminuric toxæmia | 5 | — | 2 | 6 | 2 | 1 | 16 |
| Hæmorrhage | 1 | — | 3 | 1 | 1 | 2 | 8 |
| Embolism | — | 1 | 3 | 2 | — | 2 | 8 |
| Shock and anæsthesia | — | — | — | — | — | 2 | 2 |
| Liver toxæmia | — | — | — | 2 | — | 1 | 3 |
| Accidental hæmorrhage | 1 | — | 1 | — | — | — | 2 |
| Cardiac failure | — | — | 1 | — | — | — | 1 |
| Nephritis | — | — | 1 | — | — | — | 1 |
| Disseminated tuberculosis | 1 | — | — | — | — | — | 1 |
| Total | 10 | 3 | 17 | 19 | 7 | 8 | 64 |

have been ruptured for forty-eight hours. Penicillin and "Sulphatriad" courses are both given, but either or both are discontinued after the bacterial flora has been determined. In this connexion the therapy may be of considerable importance to the child, which is immersed in, and to some extent respires into its lungs, the infected *liquor amnii*.

*Anæsthesia.*—Choice and skill in anæsthesia are most important contributory factors in the mortality of both mother and child. MacIntosh Marshall (1939) attributes the sweeping aphorism to Schulcz: "Deaths after Cæsarean section are due either to infection or anæsthesia." In spite of its drawbacks ether is still the most commonly used anæsthetic at the Women's Hospital. It is helpful not to commence the administration until after the patient is on the operating table and everything is in readiness to make the incision. Local anæsthesia is coming into favour as being by far the safest. Like the lower segment operation, the use for which has been extended from "suspect" cases to "clean elective" cases, local anæsthesia is being extended from the "poor risk" patients to normal patients. In general, that which is good for the "bad" patient is even better for the "good" patient.

TABLE IV.
*Fœtal Wastage.*

| Period of Five Years. | Cæsarean Sections. | Fœtal Deaths (Stillbirths and Neonatal Deaths). | Incidence. |
|---|---|---|---|
| 1919 to 1924 .. | 164 | 43 | 26·2% |
| 1925 to 1929 .. | 135 | 19 | 14·1% |
| 1930 to 1934 .. | 212 | 25 | 11·8% |
| 1935 to 1939 .. | 285 | 44 | 15·4% |
| 1940 to 1944 .. | 284 | 55 | 19·4% |
| 1945 to 1949 .. | 638 | 79 | 12·4% |
| 1919 to 1949 (thirty years) .. .. | 1718 | 265 | 15·4% |

*Gastric Aspiration.*—Linked with anæsthesia is the pre-operative preparation of the stomach. Obstetric patients are often poorly prepared and inclined to vomit, both during induction of anæsthesia and in convalescence. The use of small indwelling tubes with suction has made a contribution.

*Anticoagulant Therapy.*—Pulmonary embolism as a cause of death could be added to make a triad with Schulcz's infection and anæsthesia. Anticoagulant therapy, therefore, would seem logical, and at the Women's Hospital a special regime is in operation. Anticoagulants have been given post-operatively in all cases of Cæsarean section since July, 1948. In more than 250 cases so treated there have been no deaths and no significant thrombotic or embolic manifestations with the little disabilities directly due to the method. In the previous thirty years there were eight embolic deaths—one-eighth of the total—and many other non-fatal embolic and thrombotic manifestations. The prophylactic use of anticoagulants involving some of this series of cases was the subject of a paper by W. McI. Rose (1949).

*Operative Technique.*—Although carried along with the general advances in medicine, the obstetrician can justly claim a large share in progress. The abandonment of the upper segment classical technique in favour of the lower segment operation is, I believe, the greatest factor in reducing the mortality rate. We may well ask whether the classical operation has any place. The answer is—only under exceptional circumstances. It has no place in the elective case or in *placenta prævia*, and the deeply engaged head can always be disimpacted if necessary through the vagina by an assistant's hand. There are some cases of contraction ring and complicating myomata in which the incision must be planned. Classical incision may be the best in Cæsarean hysterectomy and in some cases of transverse presentation of a large child. Cæsarean hysterectomy is rarely justifiable for reasons of infection alone, and the extraperitoneal approach is of very doubtful advantage.

### *Type of Operation.*

The operation as performed in this series is set out in Table V.

The outstanding point is the decline in the classical and the rise in the lower segment operation. The lower segment technique overtook the classical about seven years ago and now threatens to exclude it. The slight increase in the classical operation in the last year is due to a decision of the staff to treat some cases of *placenta prævia* by this method for purposes of comparison. The 80 recent extraperitoneal operations were performed exclusively by one member of the staff as a matter of preference rather than on indications of severity. There was one death in the 85 cases. No other member of the staff undertook to gain the necessary technical skill to become proficient. It would seem that the technical difficulties of the extraperitoneal approach outweigh any theoretical advantages, while the Porro operation should be performed for uterine rupture or myomata rather than for established or threatened infection. It is interesting to note that the first lower segment operation in this series—perhaps the first in the hospital—and also the first extraperitoneal operation were both performed in 1922-1923 by Dr. Robert Fowler, about ten years after Krönig had made the operation popular in Europe.

TABLE V.
*Type of Operation.*

| Year. | Classical. | Lower Segment. | Extra-peritoneal. | Cæsarean Hyster-ectomy. |
|---|---|---|---|---|
| 1919 to 1920 .. | 25 | | | |
| 1920 to 1921 .. | 21 | | | |
| 1921 to 1922 .. | 31 | | | 1 |
| 1922 to 1923 .. | 47 | 1 | 1 | 2 |
| 1923 to 1924 .. | 27 | 7 | | 1 |
| 1924 to 1925 .. | 32 | 2 | | 3 |
| 1925 to 1926 .. | 23 | 1 | | 5 |
| 1926 to 1927 .. | 18 | 2 | | 2 |
| 1927 to 1928 .. | 18 | 1 | | 3 |
| 1928 to 1929 .. | 21 | 2 | | 2 |
| 1929 to 1930 .. | 27 | 2 | | |
| 1930 to 1931 .. | 37 | 11 | | 2 |
| 1931 to 1932 .. | 43 | 5 | | 1 |
| 1932 to 1933 .. | 30 | 7 | | |
| 1933 to 1934 .. | 36 | 8 | | 3 |
| 1934 to 1935 .. | 37 | 20 | | 2 |
| 1935 to 1936 .. | 39 | 10 | 2 | |
| 1936 to 1937 .. | 28 | 24 | 2 | 1 |
| 1937 to 1938 .. | 43 | 24 | | 5 |
| 1938 to 1939 .. | 21 | 27 | 1 | |
| 1939 to 1940 .. | 39 | 21 | | 2 |
| 1940 to 1941 .. | 39 | 14 | | |
| 1941 to 1942 .. | 30 | 17 | | |
| 1942 to 1943 .. | 23 | 37 | | |
| 1943 to 1944 .. | 26 | 35 | | |
| 1944 to 1945 .. | 34 | 55 | | |
| 1945 to 1946 .. | 30 | 55 | | |
| 1946 to 1947 .. | 9 | 124 | 43 | |
| 1947 to 1948 .. | 2 | 94 | 35 | |
| 1948 to 1949 .. | 17 | 138 | 2 | |
| 1919 to 1949 .. | 853 | 744 | 86 | 35 |

### *Indications for Cæsarean Section.*

The indications for Cæsarean section in this series are set out in Table VI.

I will merely state some impressions. Elective operations for disproportion, apart from "repeats", are rare, borderline cephalo-pelvic disproportion and potentially difficult forceps deliveries after trial of labour have assumed a greater importance, likewise delayed labour due to ineffective uterine action. Variations in pelvic shape apart from contraction at the brim receive more consideration. The

TABLE VI.
*Indications for Cæsarean Section.*

| Main Indication. | 1919 to 1924. | 1925 to 1929. | 1930 to 1934. | 1935 to 1939. | 1940 to 1944. | 1945 to 1949. |
|---|---|---|---|---|---|---|
| Disproportion, mechanical reasons, dystocia | 69 | 61 | 79 | 72 | 97 | 206 |
| Failure of powers | 1 | — | 2 | 5 | 4 | 17 |
| "Repeat" | 18 | 39 | 57 | 71 | 81 | 142 |
| Soft tissue obstruction | 6 | 8 | 12 | 15 | 11 | 16 |
| Malpresentation | 5 | 1 | 4 | 15 | 6 | 16 |
| *Placenta prævia* | 12 | 9 | 15 | 51 | 54 | 125 |
| Accidental hæmorrhage | 4 | 7 | 4 | 1 | — | 3 |
| Albuminuric toxæmia, eclampsia | 39 | 7 | 17 | 13 | 9 | 71 |
| Liver toxæmia, vomiting | — | — | 2 | 3 | 1 | 6 |
| Intercurrent maternal disease | 6 | — | 13 | 25 | 19 | 19 |
| To deliver live child | — | — | 2 | 4 | — | 6 |
| Miscellaneous | 4 | 3 | 5 | 10 | 3 | 11 |
| Total | 164 | 135 | 212 | 285 | 285 | 638 |

cry of twenty years ago, "I have yet to see the woman who could push the head into the brim that I could not deliver with forceps from below", has been shaken. The trend has been upwards in some malpresentations when difficulty is likely, particularly breech presentation and complications of the cord. Much greater emphasis is now placed on the obtaining of a live child. The unexpected fœtal stillbirths and neo-natal deaths even in elective cases should be remembered. Anæsthesia and anoxia are potent factors in this. The increase in *placenta prævia* has been radical in contrast to accidental hæmorrhage, in which our treatment has become totally conservative. Constitutional disease in the mother, such as cardiac disease, has declined, except in the case of *diabetes mellitus*. Combinations of lesser and part indications are often summated to make a complete justification. Preeclamptic toxæmia is frequently summated with other part indications to make a complete indication.

The indications involve more completely than any other operation the whole perspective of obstetrics and call for a high degree of judgement. "I could teach you how to do a Cæsarean section in 20 minutes, but it would take me 20 years to tell you when to do it" (A. M. Wilson). The increased scope of the operation and the multiple and overlapping indications have made the difficulty greater. Our outlook is coloured by the mortality of the past, which has imposed upon us a traditionally conservative outlook. Prior to thirty years ago, the operation was the alternative to the impossible or very difficult vaginal delivery. The period of thirty years has seen a slow change, which is becoming more complete over the last few years. The question is now whether more disabilities follow in the wake of a moderately difficult forceps delivery than after an easy Cæsarean section. The difficulty is in judgement, to decide in advance just how difficult the vaginal delivery will be.

From the figures produced it is obvious that, although the incidence is increasing, it is still over our last five years only about half that in many other centres—one in 38 against perhaps one in 16 cases. Our increased mortality rate may be explained by the selection of more serious cases. It seems likely that our tendency in the future will be towards more and earlier operations. Looking to the future, we may well ask, has this incidence reached its optimum, will the tendency progress even further, or has the pendulum already swung too far? Are we on the threshold of the surgeon's idea of obstetrics becoming a reality? "A sort of expert midwifery garnished by the Cæsarean operation" (D'Esopo, 1950).

## Conclusion.

It was the custom in Melbourne in teaching to commence any lecture on Cæsarean section by listing firstly its disadvantages. I will conclude by mentioning some of the old war-cries, even if they do not carry quite the same weight and are becoming threadbare: No operation in surgery is more commonly followed by ventral hernia. The woman is left an obstetric invalid, the size of her family is limited, and she is haunted by the bogy of subsequent rupture. The more the sections, the more the "repeats"—they make up nearly one-quarter of our indications. "The desire to do a Cæsarean section unnecessarily is a disease begot by *furor operandi* out of obstetrical ignorance" (Jellett). "There is a danger of exalting technique at the expense of sound judgement."

I have quoted three successful cases under bad circumstances; let me quote another in this series in which I operated, about three years ago. It is not often that a medical gathering has the privilege of knowing the follow-up of cases. There may be several present here who saw this operation performed at the Women's Hospital for a gathering of the Royal Australasian College of Surgeons in Melbourne.

The patient was a *primigravida*, aged over forty years, who had attended the sterility clinic and was very anxious for a child. She was a little over time, with fœtal head unfixed and borderline disproportion. I chose her in preference to another patient because she was the thinner and had no previous operation scar. The local anæsthetic took extremely well, the baby cried with its head delivered, the uterus retracted, blood loss was minimal, the patient smiled in the operating theatre, and the audience was satisfied. The puerperium was happy and uneventful, the temperature was always normal, and the patient was up and about. Late in the puerperium, when standing by the bed, she called for the nurse and died almost immediately from embolism.

Of course, we can always say we have had no deaths now from embolism since we use anticoagulants as a routine measure, and we should have allowed her to move about earlier. Who knows?

Even done as a procedure of election and under the best circumstances, the operation carries a mortality still several times greater than that of deliveries in all.

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# Reports of Cases.

## ADIPONECROSIS SUBCUTANEA NEONATORUM.

By J. M. O'DONNELL, M.B., Ch.M.,

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### Clinical Record.

R.C., a female child, was born normally on July 14, 1950; she weighed eight pounds nine ounces. An August 8 her rectal temperature was 98·6° F. A bluish-red area had been noticed on her back four days previously; the discoloration had persisted, but had not become more extensive; on August 8 it was noticed to be thickened. The child had no cough and no dyspnœa. She was breast fed every four hours, and regurgitated a little of each feed, but did not vomit. She had one to three bowel actions a day; the motions were loose and yellow and contained curds; no other changes were observed.

On examination of the child, a reddish-blue thickened area was present on the back of the thorax. The skin felt thickened and moved freely on the underlying tissues. The area had sharply defined edges. The *alæ nasi* were not moving, and no abnormality was detected in the chest. The throat was red, no neck stiffness was present, and the liver and spleen were not enlarged. A provisional diagnosis was made of (i) cellulitis or (ii) nævus.

On August 9 the patient's general condition was unchanged; the lump appeared the same as on the previous night. A provisional diagnosis of nævus was made, and the patient was referred to my skin clinic.

I examined the patient on August 9. She had a plaque of subcutaneous and nodular infiltration on the centre of the mid-thoracic region of the back; it was four inches by three and a half inches in area. The lesion was of rubbery consistency. The plaque was attached to the skin, which was dusky and erythematous; it was somewhat tender. The overlying skin was attached to it and moved with the subcutaneous tissues on the deeper structures. When the plaque was pressed from side to side it took on a coarse *peau d'orange* surface appearance; there was no pitting on pressure. In other respects the baby appeared normal and robust; no other skin lesions were present. A provisional diagnosis was made of (i) panniculitis, or (ii) *sclerema neonatorum* or (iii) *adiponecrosis subcutanea neonatorum*.

A number of investigations were carried out. The Wassermann test failed to produce a reaction. The hæmoglobin value was 98% and the erythrocytes numbered 5,000,000 per cubic millimetre; the leucocytes numbered 12,700 per cubic millimetre, 31% being neutrophile cells, 62% lymphocytes, 6% monocytes and 1% eosinophile cells. The findings were normal for the patient's age.

The plaque was treated by inunction of cod liver oil. On August 15 the lesion was breaking up, becoming more discretely nodular and not so thick. By August 23 it was resolving rapidly. By September 13 the plaque had completely resolved, leaving a normal healthy skin surface without scarring or pigmentation. The final diagnosis was *adiponecrosis subcutanea neonatorum*—a traumatic condition.

### Comment.

The negative response to the Wassermann test and the result of the blood count excluded *lues* and blood dyscrasias. The rapid involution and the nodule formation during the resolution of the lesion gave the final diagnosis of *adiponecrosis subcutanea neonatorum*. The absence of malaise, fever, leucocytosis *et cetera* excluded panniculitis. The favourable progress and disappearance of the lesion excluded *sclerema neonatorum*.

In Andrews's text-book "Diseases of the Skin" (1946) the following description of the condition is given:

> Subcutaneous fat necrosis (*adiponecrosis subcutanea neonatorum*) is a type of subcutaneous induration occurring in newborn or young infants. Whereas the clinical symptoms are similar to those in the other indurative conditions of the newborn, there is no pitting on firm pressure and the induration does not permit the skin to be pinched up in folds. The hardness is comparable to that of wood or rubber. Small nodular lesions are often found on the back, cheeks, buttocks or almost any part of the body. Softening and absorption of the indurated areas begin about the fifth or sixth week and are complete in a few months. The cause is usually trauma.
>
> Ehrmann and Brunauer separate *adiponecrosis subcutanea neonatorum* from *sclerema neonatorum*, but Gray holds that the two are identical conditions. Howard Fox has reported the study of five cases and has fully covered the differential diagnosis of the disease.

### Conclusion.

I am reporting this case because there seem to be very few reports of this dermatosis on record.

## A GLAUCOMA PROBLEM.

By E. TEMPLE SMITH,

*Sydney.*

THIS is the story of a very tragic occurrence which fortunately had a happy ending.

### Clinical Record.

A soldier of the 1914 war, aged at present sixty-five years, had lost his left eye by enemy action. In March, 1948, he came under my care for routine presbyopic correction. I found his disk slightly cupped, his visual acuity 6/9, the tension raised (30 millimetres) and a large scotoma extending to within 15° of the fixation point. This was chronic glaucoma beyond doubt. With a one-eyed man I naturally temporized with miotics as long as my conscience would allow.

But, after watching him for five months, I found that the scotoma was approaching nearer the fixation point, the tension was still 30 millimetres, and I felt it my duty to advise operation. A Lagrange procedure was performed uneventfully; he was discharged from hospital in ten days and examined at intervals. It was noticed that although he had shown no sign of iritis while in hospital, his pupil was small and secluded. His visual acuity fell to 6/18 after a time, owing, it was thought, to lens sclerosis, though, since the pupil was secluded, not much could be made out. However, he remained with useful vision and normal tension, but a thin-walled bleb had developed.

Here I must digress a little. Though in the Lagrange operation I always aim at, and generally achieve, a flat filtering cicatrix not raised above the general conjunctival level, occasionally I find myself "landed" with a bleb of the type which is a constant feature of a trephine procedure, and which some of its exponents have assured me is their *desideratum*. I consider that the bleb is due to a slight fault in technique, in that one has stripped the conjunctiva at the limbus too far forward towards the cornea and the anterior chamber, whereas one's aim in the Lagrange procedure is to open up the angle of the anterior chamber permanently, to connect it with the suprachorioidal lymph space.

To resume: sixteen months later he came in to report that his sight had suddenly "gone". I found the anterior chamber collapsed and a pin-hole perforation in the bleb.

I sent him at once to the Repatriation General Hospital, Concord, and had a sleepless night wondering how I could remedy the situation. Two days later I stitched a double-pedicled flap over the leak after scarifying the adjacent area. After a week the anterior chamber was just present, though very shallow, and one hoped the leak was sealed.

In the meantime he had developed a complete cataract and was virtually blind. However, his projection was active, so he evidently had not a detached retina, which was the complication I most feared. He then went home to await the further maturity of the cataract. A month later the leak recurred, with collapse of the anterior chamber. With little hope of success I again manipulated a conjunctival flap to cover the opening; but this time I cauterized the adjacent area with a fine cautery heated over a spirit-lamp. This was successful in sealing the leak, and a month later I extracted the swollen cataract. The chamber was so shallow that I had to use a keratome well in front of the limbus and enlarge the incision with scissors. I then performed an iridectomy, stripped the adherent iris from the lens and expressed the latter. It came out very well and, after irrigation, not much cortex was left. I was afraid to use atropine, though in the event I am sure it would have been both safe and advantageous, for there was a little hyphæmia from the vascular iris which mixed with the residual cortex and, of course, blocked the pupil.

After a week or two he began to see dimly through the occluded pupil; but as the iris showed some vascularity, I waited a month before tackling the final stage, the anterior chamber being now quite deep.

I then decided against "needling" of an elastic membrane with probable oozing from new vessels, in favour of an iridotomy performed from below. This I did, as I have described elsewhere (Smith, 1945): a wide keratome incision in the lower part of the cornea, three millimetres above the limbus, a stab with a sharp Graefe knife through the iris at the site of the lower edge of the new pupil, then the insertion of fine spring scissors (not De Wecker's), one blade in the Graefe hole and the other above the iris, one snip, and withdrawal. The result: a clear black elliptical vertical pupil.

Three weeks later, with "+11" correction and a small cylinder, he read Snellen 6/9 type and Jaeger 3 type; he can still read them. The sclerectomy is also functioning behind its conjunctival covering, and the tension is normal. Six months later he reads 6/6 and Jaeger 1.

### Conclusion.

I cannot conclude without paying a tribute to the patient's pluck and fortitude. He never lost heart or lost faith and was always cheerful. In fact, when he was totally blind for months he was the life and soul of the ward. This made my task easier. But he was no more pleased than I that I had been enabled "out of this nettle danger to pluck the flower, safety".

I publish these notes in the hope that they may be of some help to others, should they have the misfortune to meet with this rare accident. I do not expect to, as I shall make it my special care to avoid a bleb type of scar in future. But it seems to me that it may happen any day to a trephine procedure, as I understand that the bleb type of decompression scar is the aim in that operation.

### Acknowledgement.

I have to thank the chairman of the Repatriation Commission for permission to publish this case.

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## STEVENS-JOHNSON SYNDROME: REPORT OF A CASE.

By R. A. MELICK,
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THE Stevens-Johnson syndrome was described in 1922 by Stevens and Johnson, but it is stated that Alibert and Bazin described similar cases in 1822 (Rosenberg and Rosenberg, 1940, quoted by Thomas, 1950). Skin and mucous membranes are affected, and it is characterized by the presence of some or all of the following: *erythema multiforme* type of rash, penile lesions, stomatitis, conjunctivitis, bronchitis, pneumonia and urethritis. It is associated with a high temperature and prostration. Young adult males are mostly affected, and it may run a protracted course of up to thirty days. There is a tendency for the condition to recur.

Complications include corneal ulceration with permanent scarring and partial blindness (which, in some series, have occurred in a high proportion of cases), and pneumonia, usually the primary atypical type, which may be fatal.

The laboratory findings are negative and the ætiology is doubtful, though recent reports favour a virus infection as the underlying cause. Toxic and bacterial causes have been suggested.

### Clinical Record.

A young male farm labourer, aged twenty-four years, was admitted to the Royal Hobart Hosiptal on July 31, 1950, giving a history of influenza for one week and a sore mouth and throat for four days. His previous health had been excellent. His uncle and brother had suffered attacks of influenza in the preceding two weeks. Two weeks before his admission to hospital he had used for one day in the course of his farm duties an oil spray which, the manufacturers informed us, has been known to cause irritant dermatitis. He had used this spray on a previous occasion one year earlier. The illness had commenced on July 24, seven days before his admission to hospital, when he awoke with malaise, general weakness and profuse sweats. He had no pain. His condition slowly improved over the next three days, but on July 27 his throat became very painful and he was unable to eat. Later the same day he commenced to retch and cough, producing frothy blood-stained sputum. His condition remained the same until July 30, when his eyes became irritable and "sticky". He was admitted to hospital next day. There were no other symptoms referable to any system.

On examination of the patient, he was seen to be a sick young man. His temperature was 103·2° F., his pulse rate was 108 per minute, and his respirations numbered 22 per minute. He was coughing continually and producing copious amounts of frothy blood-stained bright red sputum, and his eyes were inflamed and affected by purulent conjunctivitis; no corneal ulcers were seen. The mouth and throat were covered with yellowish fibrinous exudates, and the mucosa where visible was swollen and reddened. No rash was present, the spleen was not palpable and no enlarged glands were felt. All other systems including the respiratory system were clear. His blood pressure was 145 millimetres of mercury, systolic, and 80 millimetres of mercury, diastolic. Examination of his urine gave normal results.

No Vincent's organisms were seen on a smear from a throat swab. A mixed growth was obtained on culture; no hæmolytic streptococci were grown. A leucocyte count on July 31 showed 8300 per cubic millimetre; the appearances in a blood film were normal. A full blood count on August 5 showed that the hæmoglobin value was 15·4 grammes per 100 millilitres, the leucocytes numbered 6450 per cubic millimetre and the appearances in a film were normal. On microscopic examination of the urine, no

abnormality was noted. The Wassermann and Kline tests produced negative results. On July 31 an X-ray film of the chest revealed bronchitic changes only.

He was ordered eye and mouth toilets, potassium chlorate gargles every four hours, 30% sulphacetamide eye drops every four hours, sulphadiazine (three grammes *statim* and one gramme every four hours by mouth) and penicillin (100,000 units three times daily by intramuscular injection). On August 2 small red papules about half a centimetre in diameter developed over his body and limbs, being slightly more pronounced over the extensor surfaces. These papules had small central depressions which were yellowish in colour. On the penis and scrotum these papular lesions were well developed, and many had already become vesicular and even bullous in places. By the evening he had a well-developed *erythema multiforme* rash, and the scrotal and penile lesions had burst and were weeping. His temperature was still over 102° F. and his general condition was unchanged. The penicillin dosage was increased to 50,000 units every three hours, and he was ordered "Acetylarsen" by intramuscular injection. By August 4 the rash was widespread, particularly over his back. The individual lesions had extended to a diameter of one and a half to three centimetres. The yellowish central portion had also extended, becoming vesicular and then bullous. The only painful lesions were those on the penis, which now covered practically the whole shaft, and meatal ulceration caused dysuria and retention of urine requiring catheterization. His temperature was still 102° F., and he looked very ill, the extension of the rash to his face not improving his appearance. His eyes and mouth were still the same, and he was still producing profuse blood-stained sputum. Surprisingly, he said that he felt fairly well. At this stage, penicillin and sulphadiazine therapy was discontinued, and he commenced aureomycin treatment, 500 milligrammes being taken orally every six hours. Over the next two days his temperature subsided dramatically.

On August 7 he felt better, and for the first time the eyes and throat had improved, and he had ceased to produce the blood-stained sputum. The bullous change in the rash was now almost generalized. His temperature was normal.

On August 9 he was considerably improved. The eyes, mouth and throat were quite clear, and the rash was beginning to heal and fade. The penis was still raw and painful. Aureomycin therapy was reduced to 250 milligrammes every six hours.

The patient was allowed out of bed on August 14. Aureomycin therapy ceased on August 15, and he was discharged from hospital, well, with all lesions except the penile ulcers healed, on August 18. Since then he has been examined twice, the second time about three weeks after his discharge, when he was perfectly well, and the penile lesions had almost completely healed. He bore brown patches on his skin from the ulcerating bullæ, but these were fading.

### Comment.

Thomas (1950) maintains that this syndrome is a severe type of *erythema exudativum multiforme* (of Hebra), the penile lesions being an almost constant feature of the more severe cases. He suggests that *erythema exudativum multiforme* may be divided into a *gravis* type (*erythema exudativum multiforme*, Stevens-Johnson) and a *mitis* type (*erythema exudativum multiforme*, Hebra). In one of his cases sulphathiazole was regarded as the precipitating factor, and it was suspected in a second mild case. Thomas thinks that this supports the toxic theory of ætiology, at least in some cases. Stanyon and Warner (1945) called this condition "muco-respiratory syndrome", and regarded it as probably a virus infection, one common manifestation of which may be a rash (only nine of their seventeen patients developed any rash). They stress the fact that primary atypical pneumonia may develop, and this influences the prognosis. In their two fatal cases the patients died of pneumonia, which was resistant to penicillin and sulphadiazine.

### *Treatment.*

Penicillin and sulphonamide drugs have been used, and success with them has been reported in some cases, and failure in others. There can be no doubt of their value in preventing secondary infection of ulcerated bullæ. Recently aureomycin has been tried, apparently with great success. Robinson (mentioned in an annotation in the *British Medical Journal*, 1950) reported eight out of nine cases of *erythema multiforme* cleared up in three to eight days with aureomycin, while Church (1950) and Lynas (1950) have reported good results in the *gravis* type.

In the present case, aureomycin produced quick and gratifying improvement, and no permanent corneal scars developed. This response to aureomycin is regarded by recent writers as further evidence that a virus is the cause of the condition. The foregoing experience tends to confirm this.

### Summary.

1. The Stevens-Johnson syndrome is described.

2. A case of *erythema exudativum multiforme* (Stevens-Johnson type) is reported, and references to recent literature are given.

3. The ætiology and treatment are briefly discussed.

4. A viral causation is suggested.

### Acknowledgements.

I wish to thank Dr. R. Whishaw under whose care this patient was admitted to hospital, and Dr. J. C. Laver, superintendent, for permission to publish this case, and for helpful advice and criticism.

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## PERFORATION OF A SIMPLE ULCER OF THE ASCENDING COLON.

By JOHN C. BELL ALLEN, F.R.C.S. (England),
*Sydney.*

IN view of the rarity of the condition, the following case warrants recording.

### Clinical Record.

A male patient, aged forty-six years, was examined on August 25, 1949, on account of pain in the right iliac fossa accompanied by nausea. He said that two days previously he had attended a party and had felt far from well on August 24, but considered his indisposition to be a normal sequel of the said party. There was nothing relevant in his past history, except that a right inguinal hernia had been repaired and his appendix removed in 1945.

Examination of the patient revealed tenderness fairly high in the right iliac fossa above the existing appendix scar. By the following morning his pain had increased in severity and a mass could then be felt in the right iliac fossa; his bowels had acted and the patient reported passing a quantity of blood with his motion. A diagnosis of a perforation of the ascending colon was made, and it was considered that a foreign body, such as a tooth-pick, commonly used at cocktail parties, was the probable cause.

An exploratory laparotomy was carried out through a right pararectal incision; the ascending colon just above the caecum was thickened and œdematous and firmly adherent to the posterior abdominal wall. In the centre of this thickening, about two and a half inches above the ileo-caecal junction, could be felt an ulcer crater. The colon was mobilized on the lateral aspect, and an abscess cavity containing pus and fæcal material was opened. It was then found that the ulcer had perforated at this site. The amount of induration was such that it was considered impossible to perform a local resection, and consequently a right colectomy was carried out, the lower part of the ileum being anastomosed to the transverse colon. During the latter stages of the operation a blood transfusion was given.

In the convalescent period the patient suffered a fair amount of abdominal distension, which was relieved with a Ryle's tube. He later developed some wound infection, which cleared up satisfactorily, and his subsequent progress has been uneventful.

Examination of the specimen revealed an ulcerated area of a size readily admitting the index finger, having the appearance of a simple ulcer with a surrounding area of inflammatory œdema.

Dr. C. H. Shearman reported on the section as follows:

> Microscopic sections show this to be inflammatory only. No evidence of T.B. was found and no evidence of malignancy. There appears to be an abscess in the adjoining part of the wall of the caecum, but this is more likely part of the inflammatory reaction and hardly explains the cause of the condition.

**Comment.**

In the absence of an appendix there appeared to be little alternative to a diagnosis of perforation of the ascending colon, in view of the sudden onset, pain, mass and tenderness. The fact that the patient had been in normal robust health prior to the onset of his present condition tended to exclude the possibility of a carcinoma, and a perforation by a foreign body appeared the obvious conclusion. At operation, in spite of a careful search, no foreign body was discovered, and it must consequently be considered that the condition was an acute simple ulcer, for the presence of which no explanation can be offered.

In a limited search of literature no record of a similar case has been found.

## Books Received.

*[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]*

"Cleft Palate and Speech", by Muriel E. Morley, B.Sc., F.C.S.T., with a foreword by Professor T. P. Kilner, C.B.E., F.R.C.S.; Second Edition; 1951. Edinburgh: E. and S. Livingstone, Limited. 7" × 5", pp. 184, with many illustrations. Price: 12s. 6d.

The first edition was published in 1945.

"Virus and Rickettsial Diseases", by S. P. Bedson, M.D., F.R.C.P., F.R.S., A. W. Downie, D.Sc., M.D., F. O. MacCallum, B.Sc., M.D., and C. H. Stuart-Harris, M.D., F.R.C.P.; 1950. London: Edward Arnold and Company. 8½" × 5½", pp. 396, with some illustrations. Price: 24s.

Intended to make good the deficiency between the findings of virus research and the time when those findings become general knowledge.

"The 1950 Year Book of Pediatrics (July, 1949-July, 1950)", edited by Henry G. Poncher, M.D., with the collaboration of Julius B. Richmond, M.D., and Isaac A. Abt, M.D.; 1950. Chicago: The Year Book Publishers, Incorporated. 7½" × 5", pp. 516, with some illustrations. Price: $5.00.

One of the Practical Medicine Series of year books.

"The Neurologic Examination: Incorporating the Fundamentals of Neuroanatomy and Neurophysiology", by Russell N. DeJong, M.D.; 1950. New York: Paul B. Hoeber, Incorporated. 10" × 7", pp. 1098, with 368 illustrations. Price: $15.00.

Intended as a practical guide to students and practitioners.

"Handbook of Child Health", by Austin Furniss, L.R.C.P., L.R.C.S. (Edin.), L.D.S., D.P.H. (Univ. Manchester); 1950. London: Sylviro Publications, Limited. 7¼" × 4¾", pp. 284. Price: 25s.

Intended to be "a review of the main features of child health"—the emphasis is on health and not on disease.

"Aids to Botany", by H. J. Bonham, B.Sc.; Third Edition; 1950. London: Baillière, Tindall and Cox. 6¼" × 4", pp. 240, with some illustrations. Price: 6s. 6d.

One of the practical aids series intended for the use of students.

"Aids to Orthopædic Surgery and Fractures", by I. E. Zieve, M.A. (Cape Town), F.R.C.S. (England); Third Edition; 1950. London: Baillière, Tindall and Cox. 6¼" × 4", pp. 300. Price: 6s. 6d.

One of the well-known practical aids series, intended for the use of students.

"Physics in Medical Radiology", by Sidney Russ, C.B.E., D.Sc., F.Inst.P., L. H. Clark, Ph.D., F.Inst.P., and S. R. Pelc, D.Ph.; Second Edition; 1950. London: Chapman and Hall, Limited. 8½" × 5½", pp. 306, with some illustrations. Price: 25s.

The first edition was published in 1928; this edition has been largely rewritten.

"Injuries of the Knee Joint", by I. S. Smillie, O.B.E., Ch.M., F.R.C.S. (Ed.), F.R.F.P.S.; Second Edition; 1951. Edinburgh: E. and S. Livingstone, Limited. 9½" × 7", pp. 408, with many illustrations, some of which are coloured. Price: 50s.

A revision of the monograph published in 1946.

"Differential Diagnosis of Internal Diseases: Clinical Analysis and Synthesis of Symptoms and Signs", by Julius Bauer, M.D., F.A.C.P.; 1950. New York: Grune and Stratton, Incorporated. 9" × 6¾", pp. 888, with many illustrations. Price: $12.00.

The author "attempts to train and stimulate clinical thinking and judgment" and not to be content with the compilation of facts.

"Modern Abnormal Psychology", edited by W. H. Mikesell; 1950. New York: Philosophical Library, Incorporated. 9" × 6", pp. 896. Price: $10.00.

Designed to meet the interest of the general reader in abnormal psychology.

"A Handbook on Diseases of Children: Including Dietetics and the Common Fevers", by Bruce Williamson, M.D. (Edin.), F.R.C.P. (London); Sixth Edition; 1951. Edinburgh: E. and S. Livingstone, Limited. 7¼" × 5", pp. 454, with many illustrations. Price: 17s. 6d.

Last revised in 1947.

"Hospital Improvements: How to Improve the Daily Life of the Patient in the Ward", by Olive Matthews; 1950. London: 22 Harrington Gardens, S.W.7. 8¼" × 5¼", pp. 32, with some illustrations. Price: 1s. 6d.

Illustrated by the author.

"A History of English Public Health, 1834-1939", by W. M. Frazer, O.B.E., M.D., M.Sc., D.P.H.; 1950. London: Baillière, Tindall and Cox. 9¼" × 6¼", pp. 518, with 16 plates. Price: 35s.

Deals with the most interesting period of British social history.

The Medical Journal of Australia

SATURDAY, FEBRUARY 3, 1951.

*All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.*

*References to articles and books should be carefully checked. In a reference the following information should be given without abbreviation: surname of author, initials of author, year, full title of article, name of journal without abbreviation, volume, number of first page of the article. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.*

*Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.*

## THE TRAINING OF PHYSICIANS AND MEDICAL TEACHERS.

In July, 1946, the training of teachers in clinical medicine was discussed in these columns; reference was made to a report on medical education by the Planning Committee of the Royal College of Physicians of London, and to an address given by Professor M. B. Capon to the Section for the Study of Disease in Children of the Royal Society of Medicine. In the first document we were informed that when appointments are made to the clinical staffs of teaching hospitals in Great Britain, "choice is made on a variety of grounds, including clinical ability, personality, contributions to new knowledge and ability to teach". In a reference to the "Goodenough Report" it was noted that the ideal teacher had a wide and sound knowledge of his subject—if he was a clinical teacher, his knowledge of medicine was allied to skill of a high order in medical practice. "He has a keen interest in students, their development and their ideas, and an ability to inspire and guide them as well as to instil knowledge into them." In a recent tribute in these columns to Professor Peter MacCallum on his retirement from the chair of pathology in the University of Melbourne, the teacher in medicine was described as being always a student and as travelling the same road as those whom he taught, leading and directing them, but endeavouring all the time to widen his own horizon, enlarge his own experience and increase his own knowledge. Professor Capon, it may be remembered, put forward the idea of an experiment which might be started in one or two university centres. He thought that several senior teachers, aided by one or two preclinical teachers, and by the professor of education, might hold preliminary discussions and arrange a vacation course for junior clinical teachers. If this kind of thing was done, it would mean that medical teachers of the future would be taught how to teach. We know only too well that when a young graduate, fresh from post-graduate study courses and possibly in possession of a newly acquired higher degree or specialist diploma, is appointed to the staff of a teaching hospital in this country, it is assumed that he can teach and he is at once provided with groups of students who hang on his words and hope that they are words of wisdom. If any plan such as that suggested by Capon was put into effect, the prospective teachers would at least ask themselves whether they had any teaching ability. It might also have the effect of inducing those who make appointments to teaching hospital staffs to pay more attention to teaching ability than they do.

Those who are interested in this subject will find food for thought in an address delivered in April, 1950, to the annual meeting of the American College of Physicians by Dr. Henry A. Christian.[1] The title of his address was "Present Day Undesirable Trends in the Training of Physicians and of Teachers of Internal Medicine". Christian is one of the well-known senior physicians of the United States. He mentions that he retired from activity in hospital and teaching work eleven years ago; he is best known to Australian practitioners perhaps as having succeeded a few years ago to the editorship of what was originally Osler's "Principles and Practice of Medicine". Christian names the three influences which determine the type of training that a young man will seek when he has left the medical school and after he has determined to make of himself an internist and possibly a teacher of internal medicine. He places first in importance the guidance, conscious or unconscious, of some of his teachers with whom he has come into some considerable degree of personal contact and whose mannerisms he often has begun to imitate. Next in importance come the organization of the hospital medical clinic in which he has chosen to work, and the personality and interests of its chief and of its other staff members. Thirdly Christian places the personality, characteristics and individual capacities and preferences of the young man himself and what he has fixed as his own particular goal in medicine. Christian does not mind whether the order of importance stated by him is generally accepted, but insists that the existence of the three groups should be recognized. Most readers will accept the three groups, but many may place Christian's third group of factors first because the individualism of the present-day medical practitioner manifests itself at a very early stage in his career and young men today are possibly more critical of their seniors than they used to be. Christian discusses the type of man who is a professor of internal medicine and chief of a medical clinic in a teaching hospital, and states that too often he is a clinical scientist rather than a clinician—more a specialist in some single field of internal medicine than one broadly conversant with the lore and the practice of medicine. It is, he holds, a disadvantage if, as chief of the clinic, the clinical scientist is not sufficiently well equipped to give to the hospital patients the best possible type of treatment; the treatment should be that likely to train the resident staff to become superior clinicians. This is, of course, one of the most difficult problems of the present-day teaching of medicine—to combine clinical science and true clinical medicine. Those who have followed the growth of clinical medicine in the last two or three decades must recognize more and more the need for the development and the teaching of what the late Thomas Lewis so well called

[1] *Annals of Internal Medicine*, September, 1950.

clinical science, but they know also that they must keep their feet firmly planted on the fundamental plank of the welfare of the patient. Christian was a pupil of William Osler, and at the end of his address he quoted Osler: "In the natural method of teaching, the student begins with the patient, continues with the patient and ends his studies with the patient." We do well to remember that Osler also wrote: "To the physician particularly a scientific discipline is an incalculable gift, which leavens his whole life, giving exactness to habits of thought and tempering the mind with that judicious faculty of distrust which can alone, amid the uncertainties of practice, make him wise unto salvation." Thomas Lewis's views on clinical science were discussed in these pages on December 15, 1934. We may perhaps at this stage conclude that when teachers of medicine are taught to be teachers, the true perspective of the application of clinical science and the welfare of the patient will be maintained. Some words of Christian may be quoted:

> Only when patients are receiving the best possible treatment, with every possible consideration given to their needs and preferences, should any other of the activities of the clinic, such as teaching and investigation, be undertaken. No one who does not put the patient's interest first, from chief all the way down to the beginning intern, should be even tolerated in any clinic. Nothing ever should be done in the study and investigation of patients not considered to be primarily important in the treatment of the patient, without careful explanation of it to the patient and without obtaining his expressed consent to its being done.

One aspect of Christian's address which we cannot forbear to mention has to do with the publication of investigational work. He finds that publication is regarded as the surest path to academic preference, and he thinks that when appointments are made too much importance is attached to a list of publications. Here again we have to be careful. New work should be recorded and, further, the publication of important original observations is about the only way in which a practitioner can let his brother practitioners know what he is doing. It is a legitimate form of intraprofessional advertising. We may be quite certain that an observer who was at great pains to keep to himself any observations that might be of assistance to other clinicians, would soon earn the opprobrium of all practitioners. But Christian sets his face against the devices adopted for the development of a personal bibliography and many of his statements are right. He uses such terms as a "game" and a "racket". He disapproves of the subdivision of papers into many parts, published separately under individual titles which give an idea of unjustified originality. Another objectionable feature in his eyes is multiple authorship—when half a dozen or more authors are listed to one article. So-and-so *et al.* become quoted so often that *et al.* "is going to become in future the most prolific contributor to medical literature as recorded in our indexes and bibliographies". Christian mentions a "race for investigational publicity" and he has some justification for his remarks. Another absurdity which we would add is the length of the list of names appearing under "acknowledgements"—even the typist gets a mention sometimes. But here we must stop.

Those who can do so, should study Christian's address. He may seem to be too conservative, but this is not really a fact. His conservatism is healthy and should stimulate thought among those who have to do with medical teachers, their procurement and their choice to fill vacancies in universities and teaching hospitals.

# Current Comment.

## FITNESS AND A C3 NATION.

THE problem of what constitutes physical fitness or, more difficult still, health is no new subject in these columns. Last year lengthy reference was made to medical classification in the services and in civil life in the light of a thoughtful and provocative paper by John W. Todd (see THE MEDICAL JOURNAL OF AUSTRALIA, April 1 and May 13, 1950). Perhaps the strongest impression left by Todd's valiant effort to clarify and simplify the subject of standards of fitness and their determination is that the subject is confused and difficult and that a satisfactory answer to the problem is yet to be found. However, Todd's view that the standard of fitness is the capacity of the individual to carry out what is required of him, while a gross oversimplification, is sound as a generalization; much confusion would be saved if it was always borne in mind. It is certainly relevant to an aspect of the question not considered in our comments on Todd's paper—namely, the public consternation about the nation's fitness that has more than once arisen when details have been published of the numbers rejected as "unfit" in enlistment medical examinations. The impression produced has been of the following type:

> Here on a continent reputed to contain a race of relative giants with athletic prowess which made itself manifested in the Olympic Games, football, hockey and all the bruising activity connected therewith, did we find almost half the population to be physically below fighting form.

The quotation might well have been applied to Australia, with its considerable physical self-consciousness, but in fact it refers to North America. The words are those of the Medical Director-General of the Royal Canadian Navy, Surgeon Captain A. McCallum,[1] and epitomize the reaction in Canada and in the United States to statements issued early in the second World War of the considerable numbers who had been found unfit for the highest service medical category. Statistics of this kind have received publicity in many countries, including our own, and good use has been made of them by those anxious to demonstrate the "decadence" of the democratic nations. However, as McCallum is at pains to make clear, statistics without adequate interpretation can be most misleading, and the resulting general feeling of uneasiness has been "quite unjustified". The inference that "if a population was not Category 'A' it was unhealthy", he states, "is obviously due to lack of discrimination between the term 'fitness for military service' and the word 'health'". The defect that removes a man from Category "A" may not debar him from doing a useful job in some section of the service concerned and may be of no practical consequence whatever in the civil sphere. So far as the navy was concerned, the figures were apparently not bad at all, and the same may have applied to the air force. The figures usually quoted are those for the army, for whose higher rejection rate McCallum suggests that there were good reasons, "inasmuch as they had for final appraisal the rejectees from the other two forces and the sediment in the manpower barrel when Selective Service came into operation". Use of such figures to damn a nation as "physically C-3" is fallacious, and less complimentary words might be thought of to describe their use (as has occurred in both Canada and the United States) by those advocating State-controlled medicine, the inference being that the poor health standard was the fault of the medical profession. We need not follow the details of the fallacy given by McCallum, but those with even an elementary knowledge of the matter will be able to work many of them out for themselves. Two factors may, however, be mentioned that contributed to an unnecessarily high rejection rate: lack of experience on the part of examining medical officers with a tendency to adhere rigidly to the physical standards laid down in

[1] *The Canadian Medical Association Journal*, September, 1950.

the printed instructions and undue wariness of admitting a potential pensioner. McCallum is also doubtful about the high rejection rate for emotional instability and suggests, perhaps rightly, that some of those rejected might have benefited from service conditions and acquitted themselves with distinction. "One often wonders", he muses, "whether many decorations were not won by those who were too dumb to duck, but had a strong enough urge to take on the enemy single-handed. How many such men never got a chance to win a medal because he never got past a recruiting centre!"

McCallum makes some practical suggestions about correcting the errors of the past in the event of another war and reassuring the general public on the "C-3 nation" question. The lack of trained medical men, he states, can be largely corrected by the expansion of the reserve forces (such an expansion offers its own difficulties, but that need not be brought up now); only close association with a service and servicemen will teach the medical officer what is required of a recruit. "Pulheems" and similar systems are being tried, and no doubt some such will find general acceptance, but, as McCallum puts it, "there is no substitute for common sense, sound judgement, experience and a knowledge of service life to help an examining medical officer to reach decisions as to those who may be rejected or accepted for active service when the nation is in peril". Another (and well known) point is the need to resist attempts to use the medical services to get rid of unsuitable and undesirable men; in any case a niche can often be found for the apparent misfit with consequent saving in manpower. Finally, McCallum suggests that the examining medical officer must have reasonable assurance from his director or higher authority that he is not expected to be infallible, especially with the two types on the border-line —those who are trying to be rejected and those who want to be accepted. He must be allowed to use his judgement in the light of the national situation, free from fear of a reprimand or the possibility of causing a comparatively minor expense to the public purse. Standards may need to be elastic at times. As a conclusion McCallum asks a semi-rhetorical question: "What would it profit a nation to have a physically and mentally perfect armed force, but only in such numbers as could lose a war?" Though critical comment on the detailed implications of this question spring quickly to mind, it is worthy of careful thought.

## THE NEUROTOXIC EFFECTS OF DIHYDRO-STREPTOMYCIN.

DIHYDROSTREPTOMYCIN, which is produced by the catalytic hydrogenation of streptomycin, was introduced as a substitute for streptomycin, in the hope that the well-known neurotoxic effects of that drug might be avoided. However, it has been found that the new drug is not entirely free of neurotoxicity and that its use may be followed by impairment of vestibular function, deafness or both. In an effort to learn why untoward effects occur, D. T. Carr, H. A. Brown, C. H. Hodgson and F. R. Heilman,[1] of the Mayo Clinic, have reviewed the records of all their patients whose treatment with dihydrostreptomycin was followed by neurotoxic changes. They present case histories of ten patients and point out that in nine of the ten cases the data suggest that the neurotoxic reactions were attributable to the presence of too great a concentration of dihydrostreptomycin in the blood, rather than to idiosyncrasy to the drug; the maximal concentration was greater than 60 micrograms per millilitre. Carr and his associates have found that one gramme of dihydrostreptomycin given every twelve hours is a safe dose for an adult who weighs 50 to 70 kilograms and whose renal function is normal, and that the blood serum concentration with that dosage rises to anywhere between 45·6 and 57·6 microgrammes per millilitre one hour after injection of one gramme of the drug. The higher concentrations—over 60 microgrammes per millilitre—were attributed to a total daily dose of three grammes in two cases, to a single daily injection of two grammes in three cases, to impaired renal function in three cases and to a combination of two of these factors in one case. It seems likely that a maximal daily concentration of this order continued for several weeks will frequently damage either the vestibular or the auditory system, and that ill-effects may be avoided by keeping the concentration below 50 micrograms per millilitre. To do this with any exactness is at present difficult, as a simple laboratory method of determining the concentration is lacking. The experience of Carr *et alii* is that the maximal concentration of dihydrostreptomycin in the blood serum is not always directly proportional to the daily dose per kilogram of body weight, and so they do not believe that the total daily dose should be absolutely proportional to the body weight. They doubt that a dose of one gramme every twelve hours need be exceeded, except on rare occasions. When, however, there is evidence of decreased renal function or the patient's body weight is less than 50 kilograms, the total daily dose should be reduced accordingly. Thus with discretion effective use should be possible of what H. C. Hinshaw[1] has described as "the most popular form of streptomycin therapy". Hinshaw adds something more to this picture of dihydrostreptomycin and its toxicity in a reference to two current rumours: that dihydrostreptomycin is less effective clinically than streptomycin and that it possesses a selective toxic effect on the auditory function of the eighth cranial nerve. From the available evidence, still admittedly incomplete, he finds no reason to differentiate between the two drugs in their therapeutic efficacy or in their effect on the auditory function of the eighth nerve. He emphasizes the dangers of both drugs in the presence of impaired renal function. The important point that appears to be accepted on present experience and evidence is that larger doses of dihydrostreptomycin may be given than of streptomycin with less risk of toxic effects on the vestibular function of the eighth cranial nerve.

[1] *The Journal of the American Medical Association*, August 5, 1950.

## A "BLACKOUT" ACCIDENT.

A CURIOUS but tragic accident recently reported in *The Lancet's* "Medicine and Law" column[2] will be of interest in this land of "blackouts". At the inquest into the death of an infant boy in an Essex hospital, it was stated that the child, who was aged four days, was in an oxygen tent. Suddenly the lights in the ward went out and the ward sister struck a match to see to the boy and his twin sister, the condition of both of whom had been causing considerable anxiety. The tent went up in flames. The sister turned off the oxygen and took off the tent to get at the baby, whom she took to another ward. She extinguished the flames. There was evidence that she had had plenty of experience with oxygen tents, but there was no torch available and she had not been told where any portable lighting apparatus was kept. A verdict of accidental death was recorded. The coroner expressed his strong opinion that the accident was not due to ignorance or lack of knowledge, but to the sister's preoccupation with her patients' safety; to strike a match in the darkness was perhaps an instinctive act, one done in haste with the best intentions and without thought of the consequences. He suggested that the hospital authorities should inquire into their emergency arrangements forthwith so that such an accident should not recur. Most people will agree with the coroner's attitude, especially the lack of blame attributed to the sister, but this is not the sort of accident that should happen a second time. Adequate emergency arrangements and conscious awareness of the danger should be effective safeguards.

[1] *The American Journal of Medicine*, November, 1950.
[2] *The Lancet*, December 23, 1950.

# Abstracts from Medical Literature.

## MEDICINE.

### A Slide Rule to Determine the Axis of the Electrocardiogram.

J. H. BEATTY (*Circulation*, April, 1950, Part II) describes a simple slide rule, the use of which enables one to calculate very rapidly the electrical axis of the electrocardiogram.

### Appendicitis Complicating Pneumoperitoneum.

L. F. KNOEPP (*Diseases of the Chest*, May, 1950) states that in his experience, which tallies with a report from another source, acute appendicitis occurs much more frequently in patients receiving pneumoperitoneum treatment for pulmonary tuberculosis than in the general sanatorium population. When appendicitis occurs in such patients there seems to be little or no tendency for the infection to be localized by adjacent surrounding structures.

### Status Asthmaticus.

G. PINESS (*The Journal of the American Medical Association*, March 18, 1950) discusses *status asthmaticus*, which is described as a period of intense dyspnœa lasting for two to seven days or longer, caused by an outpouring of viscid mucous into the bronchioles resulting in a serious loss of lung capacity. It does not respond to epinephrine as a rule. Clinically wheezy dyspnœa, unproductive cough, cold clammy skin, rapid and perhaps irregular pulse, and sometimes fever, are noted. Death often occurs. Physical signs are those of severe asthma. Treatment consists of reassurance with hospital care in a private room as bare as possible. Intravenous administration of epinephrine 0·1 millilitre in 10 minims of normal saline may be tried. Intravenous drip administration of 5% dextrose in distilled water should be used continuously or every three to six hours; three to five litres are given in twenty-four hours. A saturated solution of potassium iodide may be given in doses of 20 or 30 minims thrice daily; sodium iodide may be given intravenously in doses of one gramme to a litre of solution. Aminophylline, 3·75 grammes given intravenously, then 0·5 gramme given intravenously in 1000 millilitres of 5% dextrose solution over three or four hours, repeated daily for three or four days, has been strongly recommended; but the author has little faith in aminophylline. Administration of ether and oil in equal parts *per rectum* has been tried. Caffeine, three grains given orally every three to four hours, or caffeine sodium benzoate, 0·5 gramme given subcutaneously, is effective sometimes. Morphine, heroin, "Dilaudid", "Demerol" and similar drugs are contraindicated, because they depress the cough reflex and the respiratory centre and constrict the bronchial musculature. The author admits that others disagree and favour small doses of morphia. For sedation the author suggests chloral hydrate, two grammes alone or with sodium bromide, or four grammes in 60 millilitres of warm water given rectally as a retention enema, or 0·5 to 1·0 millilitre of chlorobutan given orally. Small doses of barbiturates one-quarter to one-half grain four-hourly for mild sedation are recommended.

### Phrenic Paralysis and Pneumoperitoneum.

W. FOX (*Thorax*, June, 1950) states that in persons who have undergone treatment by phrenic nerve crush and pneumoperitoneum, the movement of the mediastinum away from the side of the paralysed hemidiaphragm is an important mechanical feature. It results in an increase in the side-to-side dimensions of the lung on the paralysed side and a decrease on the unparalysed side. There is also a compensatory rib movement on the paralysed side. These factors add to the notorious difficulty of predicting the results of this form of therapy.

### Tick Paralysis.

PAUL PHILLIPS AND M. A. MURPHY (*The Canadian Medical Association Journal*, July, 1950) describe two cases of tick paralysis. Both cases occurred in five-year-old girls, and in both a single tick was found attached to the scalp. In neither of these cases had the condition progressed to true muscular paralysis, but rather there was ataxia involving the lower limbs.

### An Evaluation of Reported Poisonings by Acetylsalicylic Acid.

LEON A. GREENBERG (*The New England Journal of Medicine*, July 27, 1950) states that a review of the reported cases of death attributed to acetylsalicylic acid reveals several noteworthy features aside from the small number of cases. A large portion of them were suicides. In these, as well as in another large portion that were not suicides, the subjects consumed amounts of acetylsalicylic acid far in excess of the doses used therapeutically. In the other cases the amounts were unknown, but, from the symptoms observed, they can be presumed to have been large. In several cases of poisoning there was a history of mental disorder; in many others there were severe underlying diseases. Severe poisoning, or death from large or massive doses of any drug, whatever the reason for its consumption, is not a criterion of the possible danger in its therapeutic use. Finally, there is a conspicuous absence of reports of serious poisoning or death, other than allergic poisonings, associated with ordinary therapeutic use of acetylsalicylic acid, even when this use has been continued over a long period.

### The Salt-Depletion Syndrome following Mercurial Diuresis.

HARRY L. JAFFE, ARTHUR M. MASTER AND WILLIAM DORRANCE (*The American Journal of the Medical Sciences*, July, 1950) state that profound electrolyte imbalance may follow mercurial diuresis. Blumgart and his colleagues have demonstrated that sodium, potassium, calcium and chlorides, in addition to water, are excreted in increased amounts. Numerous recent investigations have emphasized the greater excretion of sodium following administration of mercurial diuretics, especially with unrestricted sodium intake. Poll and Stern have compared the pronounced asthenia, restlessness and muscular cramps following massive mercurial diuresis in subjects of Addison's disease. Patients with chronic glomerulonephritis with preponderant salt loss have a similar asthenia. These symptoms may be attributed to the loss of sodium chloride. Another factor contributing to asthenia may be the loss of potassium. Urinary loss is one of the important routes for potassium excretion. With such large quantities of fluid excreted during intensive diuresis, the possibility of potassium depletion must be considered very real.

### The Reticulocyte Reaction in Respiratory Insufficiency.

N. RISKA (*Acta Medica Scandinavica* (*Supplementum* CCXXXVII), 1950) has studied the reticulocytes of the peripheral blood immediately after the production of arterial hypoxæmia by various means, such as physical exercise and the insufflation of air into the pleural cavity. It was found that arterial hypoxæmia, suddenly induced, produced reticulocytosis within two hours. This reticulocyte reaction is advanced as a simple test of respiratory insufficiency.

### Diagnostic Problems in Jaundice.

FRANKLIN M. HANGER (*Archives of Internal Medicine*, August, 1950), reports that the transport of bilirubin from the blood to the biliary system is a specific function of the parenchymal cells of the liver; however, the mechanisms regulating the excretion of bile are but poorly understood. Jaundice may be caused by a disorder leading to destruction or functional derangement of the hepatic unit or to obstruction of the biliary passages, either within or without the liver. Uncomplicated obstructive jaundice usually can be distinguished from hepatocellular jaundice by the employment of a few simple tests, such as determination of the serum alkaline phosphatase level to evaluate the obstructive factor and the cephalin flocculation and thymol turbidity tests to detect the presence or absence of inflammatory or necrotizing processes within the liver. Primary cholangiolitis, chronic hepatic intoxication and neoplastic and granulomatous infiltrations of the liver, for reasons stated by the authors, often cannot be identified with certainty by the reactions to any combination of laboratory tests. Biopsy of the liver is justifiable when the diagnosis is in doubt, but surgical exploration, rather than the trocar technique, is indicated when the picture is that of obstructive jaundice.

### Cardiac Disease and Rheumatoid Arthritis.

JAMES Y. BRADFIELD AND MILTON R. HEJTMANCIK (*Archives of Internal Medicine*, July, 1950) review the literature on cardiac disease and rheumatoid arthritis. They state that during clinical study it is expected to find one in ten patients with organic heart disease, but at necropsy one of every two or three patients will display pancardiac lesions structurally indistinguishable from those commonly associated with rheumatic fever. The authors made a critical analysis of 45 patients with uncomplicated rheu-

matoid arthritis and state that they found an incidence of organic heart disease in fair agreement with published reports of necropsy observations on patients with rheumatoid arthritis, particularly if more attention is paid to equivocal cardiac signs in patients with this disorder. Patients with "rheumatoid heart disease" generally tolerate the cardiac lesions quite well, largely owing to the limitations of activity imposed by the arthropathy and to the fact that the lesions are apt to be somewhat milder in degree. Indirect evidence is strong that rheumatoid arthritis and rheumatic fever are differing manifestations of one fundamental morbid process, which is very likely allergic in character.

### Death from Spontaneous Subarachnoid Hæmorrhage.

MILTON HELPEON AND S. M. ROBSON (*The American Journal of the Medical Sciences*, September, 1950) review the subject of sudden and unexpected natural death from spontaneous subarachnoid hæmorrhage. The study is based upon the autopsy findings in 2030 cases of sudden and unexpected natural death. In this series, there were 95 cases (4·7%) of spontaneous subarachnoid hæmorrhage, of which 59 were in men and 36 were in women. With three exceptions from the earlier years of life, the ages of patients fell between the years twenty and sixty-nine. Spontaneous subarachnoid hæmorrhage was found as a cause of death relatively most commonly in late young manhood and in middle age. In the majority of instances rupture of a cerebral arterial aneurysm was the source of the lethal bleeding. In two-thirds of the cases the aneurysm was identified, but in almost one-fourth the source of the hæmorrhage could not be located. The location of 75% of the aneurysm was on the anterior and middle cerebral and the anterior communicating arteries. Diffuse subarachnoid hæmorrhage covering the base of the brain was the most common anatomical variety. Less commonly, there was a localized subarachnoid hæmatoma over the island of Reil, or a hæmorrhage into the subdural space either directly or by a break through of a hæmorrhage in the subarachnoid space. The authors state that in a few instances an aneurysm embeds itself during development in the adjacent cerebral substance, and when such an aneurysm bursts, intracerebral hæmorrhage may result usually with, but sometimes without, extension into the subarachnoid or ventricular spaces. All occupations were represented in the series. It is emphasized that dissections of the cerebral arteries should be carried out as soon as the brain is removed from the skull, while the blood clot is soft and easily removed by washing.

### Augmentation of Vasoactive Substances by Tetraethylammonium Chloride.

I. H. PAGE AND R. D. TAYLOR (*Circulation*, June, 1950) state that vasoactive substances such as adrenaline, noradrenaline, angiotonin, histamine and barium chloride exhibit augmented activity after the intravenous injection of large doses of tetraethylammonium chloride in dogs, cats, rats and man. Other substances such as pituitrin and "Paredrine" fail to do so. In one normal young girl, who suffered an unfavourable turn after an injection of tetraethylammonium chloride, her arterial pulse becoming imperceptible, intravenous injection of adrenaline caused her blood pressure to rise to well over 300 millimetres of mercury and her heart beat became very irregular. For the first half-hour it seemed more likely that she would perish from the hypertension induced by the adrenaline than from the hypotension caused by the tetraethylammonium chloride. Hepatectomy in the experimental animal reduces or abolishes the augmenting action of tetraethylammonium chloride.

### An Overdose of B.C.G. Vaccine.

J. SAIE AND J. CHEVÉ (*Revue de la tuberculose*, March-April, 1950) describe the sequel to the vaccination of a newly-born infant with B.C.G. by a midwife (*sage-femme*), who drew up the whole of the contents of an ampoule of vaccine into a syringe and injected it intramuscularly into the child's buttock. A large cold abscess developed in the buttock, but the infant did not suffer any constitutional disturbance. The abscess was aspirated and a seton inserted, and healing occurred in less than three months. Later suppuration occurred in the inguinal lymph glands, but this also settled down in less than six weeks.

### Lead in Relation to Disseminated Sclerosis.

A. M. G. CAMPBELL, G. HERDAN, W. F. T. TATLOW AND E. G. WHITTLE (*Brain*, March, 1950) discuss the place of lead as an ætiological factor in disseminated sclerosis. Their work was based firstly on the incidence of disseminated sclerosis in relationship to the lead content in the soil in various areas, secondly on examination of the soil and water content for lead in areas where disseminated sclerosis was frequent, and thirdly on estimation of the lead content of teeth in patients with disseminated sclerosis. They found that in certain areas where there was a high incidence of disseminated sclerosis, there was an increase in the lead in the soil and that in certain cases of disseminated sclerosis the teeth contained an increase of lead. They suggest that lead may play a part in the ætiology of disseminated sclerosis.

### Subacute Combined Degeneration of the Spinal Cord.

C. C. UNGLEY (*Brain*, September, 1949) discusses the treatment of subacute combined degeneration of the spinal cord. He is concerned mainly with comparing the effects of treatment by ordinary liver extracts with that of the red crystalline antipernicious anæmia factor, vitamin $B_{12}$. He concludes that vitamin $B_{12}$ is as effective as liver extract in the management of pernicious anæmia and subacute combined degeneration. This work also excludes the need for postulating a separate neuropoietic factor. The pure extract has no advantage over the usual liver extract, provided they are potent. The author suggests that a weekly dosage of 40 microgrammes of vitamin $B_{12}$ is adequate for the first six months and that then the dosage can be halved. With any signs of relapse or intercurrent infection the amount should be increased.

## THERAPEUTICS.

### Choline in Coronary Arteriosclerosis.

L. M. MORRISON AND W. F. GONZALEZ (*American Heart Journal*, May, 1950) treated 115 patients suffering from proved coronary thrombosis and myocardial infarction with choline administered orally in an average dose of 12 grammes daily for periods of one to three years after recovery from the immediate attack. Control patients, also numbering 115, who were alternately admitted into the same hospital with the same diagnosis, received no choline. The subsequent mortality rate appeared to be significantly reduced by the treatment with choline. The study suggested to the authors that the lipotropic agent choline was of value in the treatment of coronary arteriosclerosis.

### Antihistamine Drugs.

T. H. STERNBERG, D. J. PERRY AND P. LE VAN (*The Journal of the American Medical Association*, April 10, 1950) discuss antihistamine drugs. They have studied the effect of the different preparations in use by histamine electrophoresis. The results in the human being showed tripenelamine ("Pyribenzamine") hydrochloride, diphendramine ("Benadryl") hydrochloride and pyranisamine maleate ("Neoantergan") to be the most effective by this test. Phenindamine tartrate ("Thephorin"), "Diatrin", "Trimetron", "Decapryn", "Tagathen", "Thenylene", "Histadyl", "Neohetramine" and "Antistin" showed decreasing activity in the order mentioned. The study showed that different persons reacted differently. The authors state that the data correlate closely with clinical experience.

### Subacute Bacterial Endocarditis.

DAVID LITTMANN AND ROYAL S. SCHAAF (*The New England Journal of Medicine*, August 17, 1950) state that their experiences with subacute bacterial endocarditis for the years 1947-1948 were collected and compared with those for the preceding three years. The adequately treated failures, numbering 23 cases, were separately compared with the 52 successes. Early recognition and adequate antibiotic therapy were important in obtaining cures and limiting permanent structural damage. Most deaths (17 of 23) occurred as a consequence of irreversible cardiac, renal or cerebral changes despite sterilization of the bloodstream. Infection was present terminally in only six cases, and in four of these was considered to be due to truly resistant organisms. The nutritional state of the patients was found to be of prognostic value. In approximately half the failures the patients were poorly nourished, and only 6% of the cured patients were so designated. Uræmia and congestive failure were ominous events during the course of subacute bacterial endocarditis and commonly foreshadowed an unsuccessful termination. Patients with the most serious heart disease fared the least well. There was a relatively high incidence of congenitally bicuspid aortic valves among those who died.

# British Medical Association News.

## SCIENTIFIC.

A MEETING of the New South Wales Branch of the British Medical Association was held at Broughton Hall Psychiatric Clinic, Leichhardt, New South Wales, on December 7, 1950. The meeting took the form of a series of clinical demonstrations by the medical superintendent, Dr. Guy Lawrance, and members of the staff of the clinic. Parts of this report appeared in the issues of December 23, 1950, and January 13 and 20, 1951.

### Paraphrenia.

A group of patients was presented suffering from paraphrenia of the amorous and the persecutory types. The first, a single woman, aged forty-three years, a domestic servant, had been admitted to the clinic on October 4, 1950, because she felt that people were passing through her to each other and she feared injury at their hands. Since the death of her mother eighteen years earlier she had been at loggerheads with the family members because of her fancies. She dreamed the fancies, but as dreams she claimed that they were real. She used to hear voices, and put that down to mental telepathy. She was afraid to go to sleep because she had sexual dreams, and on waking she felt sure that sexual intercourse had taken place. She felt an after-image of external pressure against her body, but not of any internal pressure. She said that people talked about her having a man in her bed, but how they knew that she would not say. She had been in love with a man who had not returned the affection, because he had no idea that it existed. He married another girl, but the patient claimed that he was the man involved in her dream, and she felt that she was depriving another woman of her marital right. She had episodes, which might last as long as three weeks, when her fantasies were strongly exhibited and she felt that she was widely discussed. At times she could name the tormentors. She often listened for voices and knew that she was being defamed. At night she had locked herself in her bedroom to avoid people. Recently she had taken an overdose of sedative tablets with suicidal intent. She lay awake at night wrestling with her sexual ideas, and under that stress she had been told by voices to attack someone whom she loved—in fact, the former love object, the man. Her early days had been spent in the country, and she was an expert rider and could handle cattle well. She liked men's work and was fixated upon her father. As a result she was still single. The comment was made that the patient had actual strong sex urges, but had never taken any steps about the matter. Her repressed longings were showing themselves in the form of dreams, fantasies, hallucinations *et cetera*. She was having a course of electro-convulsive therapy, and some insight therapy was being given her; but it appeared that the symptoms of her illness were too dear to her to be cast aside for the uninteresting reality. Her personality was fairly well preserved in other directions, and there was hope that eventually she might be able to carry on with a social cure.

The next patient, a single woman, aged thirty-four years, had been a clerk and salesgirl. She had been admitted to the clinic on October 3, 1950, because she expressed the belief that her mind and body were controlled by a man whom she had not seen for eighteen months. She was afraid that she would die because of the influence. She had been engaged several years earlier, but broke off the affair about a year before the time of her admission to the clinic. She felt that her employer had obtained control of her brain, and she experienced a blackout. It had begun as control over her sexual apparatus, and she experienced the same sensation as if a man was in her bed. She could feel the weight of his body pressing against hers, but always outside; no penetration took place. She felt sure that that had made him ill, because he had never been able to obtain relief by ejaculation, and she had nearly died from the effects of that also. She had auditory hallucinations and received messages from the man, and she found things very mixed. She heard voices of people discussing her relations with the man, and believed that many people knew all about the matter. She had been worried for some months, had given up going out, had lost her appetite and could not sleep. She had begun to take a proprietary bromide preparation and to indulge excessively in cigarette smoking. Recently she had expressed a strong desire to commit suicide. She had given up work and had sought relief. Her mother was "nervy", one of her sisters was a mental defective, and her maternal aunt had had several "nervous breakdowns". The patient's early life had been satisfactory, and she had reached intermediate standard at school. She was good at music and had passed high-grade examinations. She was a poor social mixer and was self-conscious, but she swam and played tennis. At the age of eighteen years she had had an hysterical illness, but made a good recovery. Her father had died twelve years before the time of her admission to the clinic; she had lived with her mother, who opposed her wishes and tried to restrict her in her interest in men. The comment was made that the patient was a shy, retiring girl who had been severely restricted by living for years with a dominant mother, who had tried to build up an atmosphere of nun-like purity for them both. The patient had obeyed to some degree, but her unconscious sexual urges had exerted their power and had been repressed. At the present time they had come out in full force. Quite a florid symptomatology had been built up with projection directing the make-up, and a man had been introduced. The patient admitted that the man never took any notice of her, and that he had married another girl; yet she attributed all her sexual worries to him and lacked insight by which she could see the folly of her ideas. She was having electroconvulsive therapy and discussions along psychotherapeutic lines, but her recovery was problematical. It might be possible to calm her troubles so that she could resume work for a time.

The third patient in the group was a married woman, aged forty-two years, who had three children. She had been admitted to the clinic in August, 1950, because she expressed delusions of persecution associated with hallucinations. Since the birth of her last child three years previously she had had bladder trouble, for which she did not seek aid, as she was unwilling to display her perineum to anybody. Finally, in May, 1950, she had an operation for perineal repair. Five days later she expressed a delusion that people were taking photographs of her private parts, and that the people in the hospital were trying to harm her by drugging her and spraying ether over her. After she left the hospital those ideas returned. She had auditory hallucinations and heard people talking about her, and she smelt ether on her body. She expressed ideas of *déjà vu*, and claimed to have met strangers often before. Before the operation she had been frigid, but after it she had been like a nymphomaniac. She denied that she was married, she expressed fears that she had betrayed people, and she felt much guilt about what she had said while she was under the anæsthetic. She was unable to carry on at home. Investigation revealed that her father, although an alcoholic, had brought up his family on strict religious lines. The girls were well guarded and taught to regard sex life as filthy and degrading. The patient felt that the contamination had been sinful and enforced strict *coitus interruptus*. All her life she had been a sensitive, superior person and had held aloof from many pleasures of life. At the present time she was labile in her emotions, depressed at times and at others aggressive and intolerant. She was restless at night, when the delusions came on at their strongest, and she was distinctly asocial. The comment was made that there could have been a psychopathic element derived from the father's side of the family. The patient had had chorea after rheumatic fever at the age of sixteen years; with it had been associated delusions of persecution and of electrical interference, as well as hallucinations. It seemed probable that she had had a schizoid episode at that time, that her present paraphrenia was a late recrudescence of the weakness in her personality, and that she could be expected to deteriorate more rapidly. Her experiences at the recent operations could act as a precipitating factor. She had had a course of electro-convulsive therapy, but had not responded very well. Insight therapy was not proving very helpful. The treatment would be persisted with, although, as paraphrenia was a deteriorating disease, the patient's outlook was not very satisfactory.

The last patient in the paraphrenic group was a married woman, aged forty-eight years; she had two children and had been divorced. She had been admitted to the clinic on September 29, 1950, because she expressed delusions that her son was an evil-doer and she had heard voices accusing him. She had been well until two years previously, when she began to accuse her *de facto* husband of being unfaithful. She made hostile remarks to him in public and quarrelled in private. She had delusions of persecution, in that she complained that the wireless and the newspapers were spreading gossip about her, and that the neighbours played rays on her head. She loved her *de facto* husband, although she was convinced that he belonged to an organization which directed things against her. She felt that her daughter

was abetting him secretly. She heard and saw persons who were spying upon her and controlling her movements. The symptoms varied slightly from time to time, but maintained the same general form. A more recent idea was that her son was raping girls and acting as a pervert. She claimed that her daughter was acting in a similar way with men. She heard her son calling for help. Investigation of her background showed that she was the eldest of six siblings in the family of a wharf-labourer, and that her earlier life had been happy. She had poor scholastic attainments. She had been divorced from her first husband because of his cruelty to her, and immediately afterwards had begun to live with the *de facto* husband. She intended to marry him, and it was a shock to her to find that he was a married man and had made no effort to obtain a divorce. He had merely played upon her affections and had betrayed her. He was the only man with whom she had achieved sexual orgasm. She was at present undergoing her menopause. It was pointed out that the mental shock of the *de facto* husband's marital status had been very severe, and she felt that everything in life had turned against her. Her menopause also had wakened her sexual urge, and that had had to remain unsatisfied. She had obtained an escape in fantasy, and was almost psychotic at times. She had had a course of electroconvulsive therapy with a short period of psychotherapy, but great progress had not been made. The outlook was not good, because the patient disliked heartily the actual truth of the conditions with which she was faced. At times she had been very depressed, restless and rather hostile, and, as paraphrenia was a deteriorating illness, her future appeared poor. In such cases suicide was often resorted to in preference to the continuation of an unsatisfactory life.

### Ulcerative Colitis.

A patient suffering from ulcerative colitis was presented because of the associated psychosomatic interest. It was explained that psychosomatic medicine was concerned with an appraisal of both emotional and physical mechanisms involved in the disease processes of the individual patient, with particular emphasis on the influence that those two factors exerted on each other and on the individual as a whole. Psychosomatic disorders had been listed as paroxysmal rhinorrhœa, bronchial asthma, gastric and duodenal ulcers, ulcerative colitis, essential hypertension, arterial degeneration with coronary artery disease, hyperthyreoidism, migraine, chronic arthritis, urticaria, pruritus, enuresis, primary dysmenorrhœa, and more recently many cases of fibrositis. The statement of Dr. H. Maudsley was quoted from his presidential address to the Section of Neurology and Psychiatry at the Australasian Medical Congress (British Medical Association), Seventh Session, May-June, 1950. In it Dr. Maudsley had pointed out that it had been said, on the introduction of the term "psychosomatic medicine", that the experienced doctor was aware of the fact that every illness had an emotional content. He thought, however, that it was only partly realized by even experienced physicians and surgeons that the more superficial anxiety, irritability and so on seen in everyday practice was not covered by the term "psychosomatic". Psychosomatic medicine dealt with psychological factors which had some ætiological bearing on the illness and which might have considerable influence on its course. The factors might not be obvious to either patient or doctor, and might be elicited only after a series of psychiatric interviews.

The patient presented was a married woman, aged fifty-three years, who had two children. She had been admitted to the clinic on May 25, 1950, because of a depressive state associated with chronic anxiety of years' duration and ulcerative colitis. A year earlier her illness had become worse. She had found that she could not talk to people or go out and do any shopping alone, as she felt that someone was watching her, and she needed friendly support. She had anorexia, and said that all food tasted alike and was rather unpleasant. Her concentration was weak and she could not repeat things in the way in which they were told to her. As a result she avoided meeting people. She was afraid of being left alone with only one person, for then there was nobody to take over the conversation; a lump seemed to come into her throat. At times she was unable to speak. She said that she had no feeling, but she often saw and heard two clocks ticking instead of one, or she saw lights duplicated. She felt that she was inadequate and unable to order goods for the home or do her housework. She claimed to have lost all natural feelings, and said that she did not feel heat or cold like an ordinary person. She could go out in the rain and keep wet clothes on and never catch cold. She cried a lot and was considerably retarded. She had ideas that people talked about her and she heard voices, but she did not know what they said. The patient's condition was considered to be a depressive state with strong paranoid trend. She was one of 15 siblings whose parents had reared them all very strictly. No parties and no young men had been allowed until the girls grew up. The patient was the youngest child and was rather spoilt. The menarche and sex were no trouble to her, as she knew all about the ways of the animals on the farm. Her early life was on the principle of "if a thing is worth doing, do it well", and she often had to re-do the family washing if the first efforts were poor. She became a perfectionist, and when she married the tendency made her house-proud. She was always full of anxiety lest things go wrong. When she was aged twenty-four years and was seven and a half months pregnant with her first child, her father was drowned. There was a suspicion of foul play, and the patient was extremely distressed. She developed a gastro-intestinal illness with vomiting, pain and severe diarrhœa. From that time she had been afflicted with ulcerative colitis. The diagnosis had been well established by expert physicians, and at times while in hospital she passed blood. It was explained that the more recent attacks had been set up by worry over her brother, who had been paying amorous attention to her daughter-in-law. Her son had ordered his uncle to stay away from the house. Also her husband was away a good deal timber-cutting. Her physical condition was satisfactory apart from the chronic ulcerative colitis. It was pointed out that feeling states characterized by anger and resentment (as at the father's possible murder in the case under discussion) were associated with hyperfunction of the colon. That set up engorgement and hypermotility, with hypersecretion of the enzyme lysozyme. The colonic mucosa became increasingly friable, and sustained feelings of anxiety with resentment would result in submucosal bleeding and ulceration. The neurosis began before the illness, and the onset of the illness usually occurred in association with some crisis in which the need of the person for tender care was threatened, typically by the loss of a parent. In the case under discussion the patient's husband was at the war and she was seven and a half months pregnant when her father was drowned. Guilt and resentment would keep the illness going. The patient felt that she was guilty in keeping company behind her parents' back, and that the death of her father in suspicious circumstances made her a very guilty person. The typical subject of ulcerative colitis was immature and often dependent and repressed feelings easily. The patient presented had had attacks of the illness whenever emotional periods had occurred in her life. The colonic reactions to emotion were those expressed by W. Grace, Stewart Wolf and Harold Wolf in an article on life situations, emotions and chronic ulcerative colitis in *The Journal of the American Medical Association* for April 8, 1950.

*(To be continued.)*

## Obituary.

### JOHN HUBBACK ANDERSON.

THE death of Dr. John Hubback Anderson at his home in North Wales has already been recorded in these pages. Although he lived in Wales for many years, he kept in close touch with his Australian friends and with Australian affairs. He acted for some years as a member of the Council of the British Medical Association for some of the Australian Branches, and was also representative of THE MEDICAL JOURNAL OF AUSTRALIA in Great Britain. He had a gift for friendship and made a host of friends during his student days and afterwards, and especially during World War I and World War II. When he suddenly appeared at a medical gathering in Melbourne as World War II was drawing to a close, the unusual and spontaneous exhibition of joy and affection with which he was received by those present was most striking to those who did not know him very well. Few members of the medical profession have been more patently sincere than he, and few more willing to do anything possible for others.

John Hubback Anderson (he was known far and wide as "Jock") was born on August 20, 1883, in Urana, New South Wales, where his father, the late J. F. Anderson, was in general practice. In 1893 the family moved to Longford in northern Tasmania. He was sent to Longford Grammar School, and in 1903 began to study medicine at the

University of Melbourne, being a resident student at Ormond College. He graduated as bachelor of medicine and bachelor of surgery in 1908, and in 1910 took his degree of doctor of medicine. While he was at the university he rowed in the Ormond College boat in several intercollegiate races in 1905, 1906 and 1907. His crew won on every occasion. He acted as senior demonstrator in the department of anatomy of the University of Melbourne in 1909 to 1911, and was appointed honorary physician to out-patients at Saint Vincent's Hospital, Melbourne, in 1911. In 1913 he became assistant to the late Dr. William Henry Lang at Corowa, New South Wales, and in 1914 took up private practice at Benalla in Victoria. On the outbreak of war in 1914 he immediately volunteered for active service, and joined the Australian Imperial Force in September of that year. He served continuously until February, 1920, in Gallipoli, Egypt and France. He served as captain in the Third Light Horse Field Ambulance with Rupert Downes, K. Aberdeen, G. E. M. Stewart, M. W. Cave and A. E. R. White. As major he was with the Seventh Field Ambulance. He later on became D.A.D.M.S. of the Third Australian Division, and subsequently as lieutenant-colonel he was A.D.M.S. at Administrative Headquarters in Horseferry Road, London. He was twice mentioned in dispatches, and in 1918 was given the decoration of C.B.E. and in 1919 that of C.M.G. In 1920 he returned to Australia and became Stewart Lecturer in Anatomy in the University of Melbourne, and he filled this position until 1923. In 1921 he acted as professor during the absence of the professor overseas, and in 1923 he returned to England.

Soon after his return to England in 1923, Anderson joined the staff of Ruthin Castle Clinic in North Wales in association with the late Sir Edward Spriggs and Dr. S. W. Patterson, who is also a graduate of the University of Melbourne. He remained a member of Ruthin staff until the time of his death. The only break was during the second World War, when he served from August, 1940, to February, 1942, and from August, 1942, to February, 1944. As lieutenant-colonel he was A.D.G.M.S. in the Military Liaison Office and later in the Australian Army Staff Office, London. He was a temporary colonel in the Australian Imperial Force in 1944. His wartime activities are mentioned in Major-General F. Kingsley Norris's contribution to this notice.

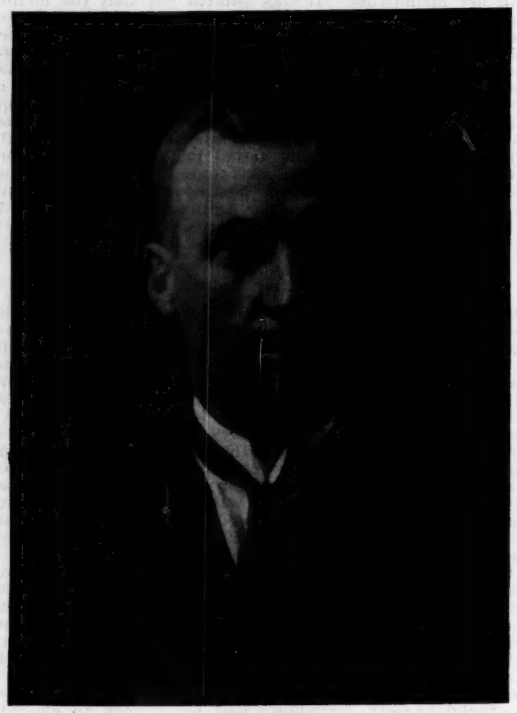
In 1940 Anderson was appointed a justice of the peace of Denbighshire, Wales, and just before his death was "pricked" as High Sheriff[1] of the County. He was probably the first Australian to hold the office of High Sheriff in Wales.

In 1946 Anderson was elected as a Fellow of the Royal Australasian College of Physicians. He always took an active part in the affairs of the British Medical Association. His membership of the Council of the Parent Body has already been mentioned. He acted for the Victorian, South Australian, Western Australian and Tasmanian Branches. Even in his early days he had taken a keen interest in post-graduate education, and was the first honorary secretary of the Melbourne Permanent Post-Graduate Committee in 1922 and 1923. He was a Fellow of the Royal Society of Medicine in London. At a recent meeting the Victorian Branch Council recorded the following minute.

> The Council of the Victorian Branch of the British Medical Association records with regret the death of John Hubback Anderson, C.M.G., C.B.E., M.D., F.R.A.C.P., sometime Senior Demonstrator in Anatomy in the University of Melbourne and later physician at Ruthin Castle Clinic.
>
> Dr. Anderson's high ideals of duty were exemplified by his service in Gallipoli and France in the war of 1914-1918, in the war of 1939-1945, by his service as Assistant Director-General of Medical Services of the Australian Army Staff in London, by his Chairmanship of the Denbigh and Flint Division of the British Medical Association from 1938 to 1941, and by his membership of the Council of the British Medical Association from 1946 to 1950, as representative of the Southern Group of Branches in Australia.
>
> Council extends its sympathy to the late Dr. Anderson's son and daughter, to his sister and to his brother, Dr. Archie Anderson.

[1] When a sheriff is appointed he is said to be "pricked". When the list is submitted to the King he "pricks" the list with a gold bodkin. This has been done for many years. There are several theories why the list is pricked. The first is that early kings could not write. Another is that the list could not be tampered with after it was pricked. A third is that Queen Elizabeth was sewing in her garden when the list was presented to her; having no pen, she seized her bodkin and pricked the list.

It was as representative of THE MEDICAL JOURNAL OF AUSTRALIA that Anderson first came into close contact with this journal. After the close of the second World War it was resolved that the practice of having a journal correspondent in England should be abandoned, and that a representative should be appointed instead. Of the enthusiasm and energy which he put into the work it is impossible to speak too highly. His "London Letters" were coloured by originality, insight, realism and humour. In many private communications he kept the Editor advised of trends on matters medical in England, and he was often able to give advance information on reports and other documents which were to appear. He kept a watchful eye on the output of His Majesty's Stationery Office and on *The Times*, London. He had an orderly mind and kept a record of his communications, always connecting something new with a preceding communication. If anything appeared in



the pages of THE MEDICAL JOURNAL OF AUSTRALIA dealing with work put out by any person or group of persons in England, he always took care to bring the comments to the notice of the persons concerned. When the Editor was in England in 1948, Anderson went out of his way to contrive meetings with persons whom he thought the Editor ought to know. It is easy for anyone connected with the running of THE MEDICAL JOURNAL OF AUSTRALIA to understand that during the war Anderson made a most effective liaison officer between London and Australia.

In 1919 Anderson married Ruby Clare, the second daughter of the late H. C. Moffatt. They had two children, a son and a daughter. Mrs. Anderson died in 1937. His daughter lived with him in North Wales, and in matters connected with THE MEDICAL JOURNAL OF AUSTRALIA she acted as an able lieutenant. His daughter and son in the Old Country, and his brother and sister in Melbourne, will, we trust, find some consolation in the knowledge of what this great-hearted man did for his profession and for individual members of it and of the high regard in which he was held.

Dr. W. G. D. Upjohn writes: There must be many Melbourne graduates who passed through the medical school in the years between 1903 and 1923 who will have heard with sorrow of the death of Jock Anderson. Though he left Australia to live in Britain nearly thirty years ago, he is remembered here with affection and respect by a great number of practitioners who had known him as a fellow student, or as a teacher of anatomy, or as a dis-

tinguished fellow officer in the Australian Imperial Force, or as a fellow practitioner initiating or actively participating in various movements designed to further the educational and other interests of the medical profession. Soon after graduation in 1908 he was appointed senior demonstrator in anatomy at the Melbourne Anatomy School where he carried out extensive anthropological research under Professor R. J. A. Berry, in addition to the regular duties of teaching anatomy to medical, dental and massage students.

As a teacher of anatomy he was excellent. He seemed naturally suited to the subject; he was exact, orderly, clear and patient in conveying instruction to his students, never dull, but introducing, where it was not inappropriate, a little wittiness in his discourse which helped to maintain the interest and attention of his audience. After the war he returned to the Melbourne Anatomy School for three years as Stewart Lecturer, 1920-1923. During the absence abroad of Professor R. J. A. Berry in 1921 he was acting professor of anatomy.

It seems likely that the mental discipline of teaching an orderly, exact, descriptive science, and the development of a personality enabling him to maintain the interest and respect of his student audiences, combined to enhance the natural traits of his character, and to fit him to carry out with such eminent success and distinction those military and civil duties which in the course of his life he was called upon to discharge.

He commenced his medical career in an academic capacity, but he never lost touch with the practising side of his profession, and, accordingly, in 1911 he applied for, and was appointed to, the position of honorary physician to out-patients at Saint Vincent's Hospital, Melbourne. However, he did not hold this position long; for when he left the Anatomy School at the end of 1911 he went to Corowa, New South Wales, to take up private practice with Dr. Lang. Later he practised at Woodend, and at Benalla, but gave up practice at the outbreak of war in 1914 to join the Australian Imperial Force as captain in the 3rd Light Horse Field Ambulance. In Egypt and Gallipoli he was closely associated with Rupert Downes, formerly a fellow student at Ormond College and his life-long, admiring and respected friend.

When the Australian Imperial Force went to France Anderson went as major to the Seventh Field Ambulance, then became D.A.D.M.S., Third Australian Division, and later succeeded Victor Hurley as his worthy successor A.D.M.S., Administrative Headquarters, London. He was twice mentioned in dispatches, and was awarded the honours of C.B.E., 1918, and C.M.G., 1919.

He married, in England, Ruby Clare Moffatt in 1919, and returned to Melbourne in the same year. Here he resumed his academic connexion with the medical school, and took an active interest in meetings of the Melbourne Pædiatric Society, and of the British Medical Association. In 1922-1923 he was a member of the Council of the Victorian Branch of the Association. He maintained a live interest in clinical work, and on Saturdays, when he was not required at the Anatomy School, he assisted me in the surgical out-patients' practice at the Children's Hospital.

Sociable, quietly cheerful, unobtrusively but persistently active, he was, for many happy years before and after the first World War, an invaluable connecting link between the university and the practising members of the medical profession. As he was *persona grata* with students, professors and practitioners, and as he had interests extending much beyond the Anatomy School, he was to a great extent responsible for a period in which the academic and practising interests in Melbourne became associated more closely than they had been, before his influence was directed specially to this end.

The result was the production of the most friendly personal relationship between the teaching staffs of the university and of the hospitals, and there grew up a lively mutual interest between the university schools and the non-academic members of the profession.

His serenely pleasant but stimulating personality and harmonizing influence were greatly missed after he had left Australia to take up his work in England, but the good work he had done here was never forgotten, and others remembered his example and endeavoured with no little success to join together the university and the teaching hospitals in furthering the interest of the medical profession in post-graduate education. Though many people and enthusiastic workers have taken their part in building the structure of the present excellent Victorian post-graduate system of instruction, it is not too much to say that a great part of the present successful combination of academic and non-academic lecturers and instructors in these post-graduate courses was due to the earlier, tactful, amiable and persistent efforts of Jock Anderson. In 1922 he became the first honorary secretary of the Melbourne Permanent Post-Graduate Committee.

He showed the same interest and helpful ability in the all-too-brief period of his visit to Australia after the end of the last war. Through his English connexions and activities he proved of the greatest help to the committee assembled by General Burston to arrange post-graduate overseas studies and scholarships for those service medical officers who had missed opportunities for such studies owing to their services to the armed forces during the war.

His strong sense of social, moral and religious duty was not expressed in talk, but showed unmistakably and characteristically in his actions. He mingled and talked with ease in mixed assemblies of men, and was as politely patient with dullards as he was alert in discussion with those of quick intelligence. His memory was good. He was quick to recognize old acquaintances whom he had not seen for years, and was ready to give them his characteristic and sincerely cheerful greeting.

During his varied and active life he engaged successively in many activities civil and military; and possessed an astonishing faculty for maintaining interest in them all. The virtue of loyalty was highly developed in him. If he engaged himself to support a cause, or an individual, there was never the slightest doubt that he would allow any private interests or feelings he might have to interfere with his loyally carrying out his engagement to the full. Faith in all that was good, loyalty, honour, sincerity, patience, charity, industry, ability and cheerfulness; these were some of the outstanding qualities which made Jock Anderson so widely respected and loved by all who had the good fortune to know him.

Major-General S. R. Burston writes: John Hubback Anderson served his country with great distinction in two wars. In World War I he proved himself as a commander, staff officer and an administrator of the highest order. Shortly after the war, he accepted an appointment to the staff of Ruthin Castle in Wales, where in the years between the wars he gained recognition in the United Kingdom as a physician of high standing.

On the outbreak of war in 1939, he immediately offered his services to the second Australian Imperial Force. The D.G.M.S., Australian Military Forces, the late Major-General Downes, who was an old personal friend of Anderson's and had an intimate knowledge of his make-up and his calibre as a staff officer and administrator in the Medical Services, lost no time in obtaining authority to bring him on the active list of the Australian Army Medical Corps in the appointment of Medical Liaison Officer in the United Kingdom. In this appointment, he was first attached to the Military Section at Australia House as a lieutenant-colonel, but in 1944, on the formation of the Australian Army Staff in London, he was attached to this staff with the rank of colonel and given the status of Assistant Director-General of Medical Services.

It would be difficult to over-state the value of this appointment to the Australian Army Medical Services and the Australian Medical Services generally. By his character, his high standing in the medical profession in the United Kingdom, his profound knowledge of army medical organization and administration, his wisdom and transparent honesty of purpose, he quickly gained the confidence and respect and, as I found on my visit to the United Kingdom in 1945, the friendship of the Director-General of Army Medical Services and his staff at the War Office, as well as the heads of other medical departments with whom he had contact in the course of his work.

He attended, by invitation, the weekly conferences of the D.G.A.M.S. and his staff, at which matters of high importance to the medical services in all theatres of war were discussed and at which the broad policy of the Army Medical Services was determined. I was informed by Lieutenant-General Sir Alexander Hood, D.G.A.M.S., that Anderson's knowledge of the organization and responsibilities of the army medical services, his clarity of vision and wise counsel were a real asset at these conferences. Moreover, the clear and fearless manner in which he put forward Australia's point of view, brought about an understanding of our special difficulties and requirements which ensured the solid backing of the D.G.A.M.S. to our requisitions on the United Kingdom for essential drugs and medical equipment. As a result, in the early stages of the war in the South-West Pacific when there was a serious shortage of all medical supplies, Australia was kept supplied with sufficient of all essentials. This enabled us to maintain a high standard of medical service both to the armed forces of Australia and to the civil community.

In addition to keeping the Army Medical Directorate in Australia informed on all important developments in the organization and administration of the medical services and other matters that would be helpful in the task of administering the Australian Army Medical Services, by his constant association with the leaders of the medical profession, he also kept us informed on all new developments and trends of thought in medicine and surgery. This information, conveyed to us in his weekly letters, many months before we could have obtained it through ordinary official channels, was one of the major factors that enabled us to ensure the efficiency of the Australian Army Medical Services.

It is difficult to give an adequate appreciation of the value of Anderson's service; so much of the work of a medical liaison officer depends on his personality, his wisdom and his capability of sifting and appreciating the information he obtains. I can only say that it would have been impossible to fault "Jock", as he was affectionately known to all of us, in this appointment.

Despite his long absence from this country, he always remained first and foremost, an Australian, with an intense love of his country. He was a great ambassador and did much to enhance the prestige of the country and the service to which he was so proud to belong and which he served so loyally.

All of us who were responsible for the administration of the Australian Army Medical Services in the war of 1939-1945 will remember with pride and gratitude our association with him during those fateful years.

Our sincere sympathy goes to all his family.

Dr. Charles Kellaway writes: Although J. H. Anderson had left Australia and made his home in Great Britain in 1923, he retained a deep interest in affairs in his native country. It was fortunate that this was so, for during the second World War he was available to act as A.D.M.S. in the Australian Military Staff in London. In the first World War after distinguished service in the field, he had served under Sir Neville Howse, V.C., at Australian Army Administrative Headquarters in London, and he therefore brought to this task a fine background of administrative experience.

At Australia House he did a very fine job, keeping the D.M.S., Australia, in touch with what was going on in the United Kingdom and placing his gifts as an excellent physician at the service of all who needed medical care in Australia House, serving on various research committees as Australian Army Medical Liaison Officer and making friends for Australia wherever he went.

It was characteristic of Anderson that everything he did was done excellently well and that he demanded the same high standard of his associates. He was a very hard worker and no trouble was too great if something needed doing, or if someone, not even necessarily a friend or acquaintance, needed help.

Jock was a sterling character, able, quick to grasp essentials, and, though a keen judge of men, tolerant of their weaknesses. He was kindness personified. He was both unselfish and self-effacing and untiring in the pursuit of what he felt to be right. It is little wonder that such a man made many friends and that wherever he went his solid worth was appreciated.

Major-General F. Kingsley Norris writes: In the United Kingdom Jock Anderson's name stood for all that is worthy in a man of service—to have known Jock, to be numbered among his many friends, was to have an immediate welcome in many places. Never sparing of himself or of his time, he was always ready and happy in his busy life to meet and to help his comrades from overseas and to present to them a clear picture of any personalities and activities in which they were interested. In July, 1950, I talked with him at Ruthven in Wales. He sounded weary, but his noble spirit still lived—it always will.

## Australian Medical Board Proceedings.

THE undermentioned have been registered, pursuant to the provisions of *The Medical Acts*, 1939 to 1948, of Queensland, as duly qualified medical practitioners:

Duffy, James, M.B., B.Ch., B.A.O., 1933 (Univ. Ireland), Belvedere Hotel, Woody Point.

Richards, William George, M.B., B.S., 1929 (Univ. London), 1928, M.R.C.S. (England), L.R.C.P. (London), 1932, M.R.C.O.G. (London), 1932, M.M.S.A. (London), 1929, 115 Logan Road, South Brisbane.

Doherty, Ralph Leonard, M.B., B.S., 1950 (Univ. Queensland), Brisbane General Hospital, Brisbane.

Green, Owen Howard, M.B., B.S., 1950 (Univ. Queensland), Brisbane General Hospital, Brisbane.

Shannon, Robert, M.B., B.S., 1950 (Univ. Queensland), Brisbane General Hospital, Brisbane.

Ahern, Edward Gilles, M.B., B.S. 1950 (Univ. Queensland), Brisbane General Hospital, Brisbane.

Barron, Vincent John, M.B., B.S., 1950 (Univ. Queensland), Brisbane General Hospital, Brisbane.

Bevan, Esther Bobbie, M.B., B.S., 1950 (Univ. Queensland), Brisbane General Hospital, Brisbane.

Bevan, Margaret Frankie, M.B., B.S., 1950 (Univ. Queensland), Brisbane General Hospital, Brisbane.

Bignold, Bernard Clive, M.B., B.S., 1950 (Univ. Queensland), Brisbane General Hospital, Brisbane.

Bridgman, Peter, M.B., B.S., 1950 (Univ. Queensland), Brisbane General Hospital, Brisbane.

Byrne, Redmond John Michael, M.B., B.S., 1950 (Univ. Queensland), Brisbane General Hospital, Brisbane.

Byth, Beatrice Averil, M.B., B.S., 1950 (Univ. Queensland), Brisbane General Hospital, Brisbane.

Cain, Patricia Mary, M.B., B.S., 1950 (Univ. Queensland), Brisbane General Hospital, Brisbane.

Donoghue, Christopher Maxwell, M.B., B.S., 1950 (Univ. Queensland), Mater Misericordiæ Hospital, South Brisbane.

Eldred, Bernice Beatrice, M.B., B.S., 1950 (Univ. Queensland), Brisbane General Hospital, Brisbane.

Finnimore, James Norman, M.B., B.S., 1950 (Univ. Queensland), Brisbane General Hospital, Brisbane.

Foote, Judith Hardwick, M.B., B.S., 1950 (Univ. Queensland), Brisbane General Hospital, Brisbane.

Foote, Peter Hardwick, M.B., B.S., 1950 (Univ. Queensland), Brisbane General Hospital, Brisbane.

Gabriel, Morgan Honesty, M.B., B.S., 1950 (Univ. Queensland), Brisbane General Hospital, Brisbane.

Grant, Rodney Edward, M.B., B.S., 1950 (Univ. Queensland), Brisbane General Hospital, Brisbane.

Harrison, Jack Robert, M.B., B.S., 1950 (Univ. Queensland), Toowoomba Hospital, Toowoomba.

Hartwig, Arthur William, M.B., B.S., 1950 (Univ. Queensland), Brisbane General Hospital, Brisbane.

Jackson, Robert Calder Sandford, M.B., B.S., 1950 (Univ. Queensland), Brisbane General Hospital, Brisbane.

Jameson, John Lee, M.B., B.S., 1950 (Univ. Queensland), Brisbane General Hospital, Brisbane.

Kelly, Leo James, M.B., B.S., 1950 (Univ. Queensland), Mater Misericordiæ Hospital, South Brisbane.

Kotowicz, Samuel, M.B., B.S., 1950 (Univ. Queensland), 70 Gray Road, West End, Brisbane.

Lang, Donald Aylmer Campbell, M.B., B.S., 1950 (Univ. Queensland), Brisbane General Hospital, Brisbane.

Liddle, William Warwick John, M.B., B.S., 1950 (Univ. Queensland), c.o. Hospitals Board, Bundaberg.

Maguire, William Brian, M.B., B.S., 1950 (Univ. Queensland), Brisbane General Hospital, Brisbane.

Meyers, Derek Harry, M.B., B.S., 1950 (Univ. Queensland), Brisbane General Hospital, Brisbane.

Meyers, John Robert Solomon, M.B., B.S., 1950 (Univ. Queensland), Brisbane General Hospital, Brisbane.

McConaghy, Nathaniel, M.B., B.S., 1950 (Univ. Queensland), Brisbane General Hospital, Brisbane.

McCrossin, Brian Maxwell, M.B., B.S., 1950 (Univ. Queensland), Brisbane General Hospital, Brisbane.

McKelvie, Ian James, M.B., B.S., 1950 (Univ. Queensland), Townsville General Hospital Townsville.

McLelland, Ian Hugh, M.B., B.S., 1950 (Univ. Queensland), Brisbane General Hospital, Brisbane.

Nelson, Geoffrey Carlyle, M.B., B.S., 1950 (Univ. Queensland), Mackay Hospital, Mackay.

O'Hara, Patricia, M.B., B.S., 1950 (Univ. Queensland), Mater Misericordiæ Hospital, South Brisbane.

O'Keefe, Victor William, M.B., B.S., 1950 (Univ. Queensland), Brisbane General Hospital, Brisbane.

Petersen, Colin Victor, M.B., B.S., 1950 (Univ. Queensland), Brisbane General Hospital, Brisbane.

Petersen, James Edmund, M.B., B.S., 1950 (Univ. Queensland), Maryborough Hospital, Maryborough.

Phillips, John Hardwick, M.B., B.S., 1950 (Univ. Queensland), Brisbane General Hospital, Brisbane.

Pigott, Louis Joseph, M.B., B.S., 1950 (Univ. Queensland), Mater Hospital, South Brisbane.

Proctor, Arthur Laurence, M.B., B.S., 1950 (Univ. Queensland), Townsville General Hospital, Townsville.

Robertson, Donald Thomas, M.B., B.S., 1950 (Univ. Queensland), Brisbane General Hospital, Brisbane.

Scott, Robert John, M.B., B.S., 1950 (Univ. Queensland), Brisbane General Hospital, Brisbane.

Smith, George Mackay, M.B., B.S., 1950 (Univ. Queensland), Brisbane General Hospital, Brisbane.

Steel, James Henry, M.B., B.S., 1950 (Univ. Queensland), Brisbane General Hospital, Brisbane.

Stumm, John Jacob, M.B., B.S., 1950 (Univ. Queensland), Brisbane General Hospital, Brisbane.

Vandeleur, Kevin Walter, M.B., B.S., 1950 (Univ. Queensland), Brisbane General Hospital, Brisbane.

Whittle, Glen Ross, M.B., B.S., 1950 (Univ. Queensland), Brisbane General Hospital, Brisbane.

Wilson, Kenneth Francis Gilmore, M.B., B.S., 1950 (Univ. Queensland), Brisbane General Hospital, Brisbane.

Wilson, Russell Gilmore, M.B., B.S., 1950 (Univ. Queensland), Cairns Base Hospital, Cairns.

Yaxley, Ronald Peter, M.B., B.S., 1950 (Univ. Queensland), Brisbane General Hospital, Brisbane.

Cumpston, Howard Bruce, M.B., B.S., 1936 (Univ. Sydney), c.o. Commonwealth Department of Health, Adelaide Street, Brisbane.

Falconer, Ian Gordon, M.B., B.S., 1950 (Univ. Melbourne), c.o. Hospitals Board, Mareeba.

## QUEENSLAND.

THE undermentioned have been registered, pursuant to the provisions of the *Medical Acts*, 1939 to 1948, of Queensland, as duly qualified medical practitioners:

Lomas, Colin, M.B., B.S., 1950 (Univ. Melbourne), Brisbane General Hospital, Brisbane.

Jones, Bruce Patrick, M.B., B.S., 1950 (Univ. Melbourne), c.o. Hospitals Board, Mareeba.

Maruff, Allan Peter, M.R.C.S., L.R.C.P. (London), 1948, c.o. Hospitals Board, Richmond.

Nally, John Brendan Aloysius, L.R.C.P., L.R.C.S., L.M. (Ireland), 1948, c.o. Dr C. W. Kingston, Pittsworth.

The following additional qualifications have been registered:

Courtice, Brian Hooper, Brisbane General Hospital, Brisbane, F.R.C.S. (England), 1948.

## TASMANIA.

THE undermentioned have been registered, pursuant to the provisions of the *Medical Act*, 1918, of Tasmania, as duly qualified medical practitioners:

St. Clair, William Alan, M.B., B.S., 1950 (Univ. Melbourne), Launceston General Hospital.

Crowther, William Edward Lodewyk, M.B., B.S., 1950 (Univ. Melbourne), Macquarie Street, Hobart.

Jones, Lindsay Henry, M.B., B.S., 1950 (Univ. Melbourne), Royal Hobart Hospital.

Gill, Peter Francis, M.B., B.S., 1949 (Univ. Melbourne), Royal Hobart Hospital.

Dudson, Keith Hewett, M.B., B.S., 1950 (Univ. Melbourne), Royal Hobart Hospital.

## DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED JANUARY 6, 1951.[1]

| Disease. | New South Wales. | Victoria. | Queensland. | South Australia. | Western Australia. | Tasmania. | Northern Territory.[2] | Australian Capital Territory. | Australia.[3] |
|---|---|---|---|---|---|---|---|---|---|
| Ankylostomiasis | * | .. | .. | .. | .. | .. | .. | .. | .. |
| Anthrax | * | .. | .. | .. | .. | .. | .. | .. | .. |
| Beriberi | * | * | * | * | * | * | .. | * | . |
| Bilharziasis | * | .. | .. | .. | .. | .. | .. | .. | .. |
| Cerebro-spinal Meningitis | 2(1) | 2 | .. | .. | .. | .. | .. | .. | 4 |
| Cholera | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Coastal Fever(*a*) | * | * | .. | * | * | * | * | * | .. |
| Dengue | * | * | * | * | * | * | .. | * | .. |
| Diarrhœa (Infantile) | .. | .. | 9(9) | .. | .. | .. | .. | .. | 9 |
| Diphtheria | 13(7) | 2 | 2(2) | .. | 9(8) | .. | .. | .. | 26 |
| Dysentery (Amœbic) | * | .. | .. | .. | .. | .. | .. | .. | .. |
| Dysentery (Bacillary) | * | .. | .. | .. | 1 | .. | .. | .. | 1 |
| Encephalitis Lethargica | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Erysipelas | * | * | * | 2(2) | * | * | .. | .. | 2 |
| Filariasis | * | .. | .. | .. | .. | .. | .. | .. | .. |
| Helminthiasis | * | .. | * | * | * | * | * | * | .. |
| Hydatid | * | .. | * | * | .. | * | * | .. | .. |
| Influenza | * | * | * | .. | * | * | .. | * | .. |
| Lead Poisoning | * | * | .. | * | * | * | * | * | .. |
| Leprosy | .. | .. | .. | .. | 7 | .. | .. | .. | 7 |
| Malaria(*b*) | * | .. | .. | .. | .. | .. | .. | .. | .. |
| Measles | * | * | * | 340(73) | * | * | .. | 1 | 341 |
| Plague | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Poliomyelitis | 59(38) | 5(3) | 16(3) | 27(22) | 1(1) | 5(2) | * | * | 113 |
| Psittacosis | * | .. | * | .. | * | * | .. | .. | .. |
| Puerperal Fever | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Rubella(*c*) | * | * | * | * | 4(4) | * | .. | .. | 4 |
| Scarlet Fever | 16(7) | 21(13) | 17(6) | 7(5) | 8(7) | 1 | .. | .. | 70 |
| Smallpox | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Tetanus | * | .. | 2(1) | * | * | * | * | * | 2 |
| Trachoma | * | .. | * | * | * | * | * | * | .. |
| Tuberculosis(*d*) | 11(8) | 15(10) | 10(6) | 15(9) | 2(1) | 3(2) | .. | .. | 56 |
| Typhoid Fever(*e*) | 1(1) | 2(1) | 2(2) | .. | .. | .. | .. | .. | 5 |
| Typhus (Endemic)(*f*) | .. | .. | 1(1) | .. | .. | .. | .. | .. | 1 |
| Undulant Fever | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Weil's Disease(*g*) | * | * | 1 | * | * | * | * | * | 1 |
| Whooping Cough | * | * | * | 9(7) | * | * | .. | .. | 9 |
| Yellow Fever | .. | .. | .. | .. | .. | .. | .. | .. | .. |

[1] The form of this table is taken from the *Official Year Book of the Commonwealth of Australia*, Number 37, 1946–1947. Figures in parentheses are those for the metropolitan area.
[2] Figures not available.
[3] Figures incomplete owing to absence of returns from the Northern Territory.
* Not notifiable.
(*a*) Includes Mossman and Sarina fevers. (*b*) Mainly relapses among servicemen infected overseas. (*c*) Notifiable disease in Queensland in females aged over fourteen years. (*d*) Includes all forms. (*e*) Includes enteric fever, paratyphoid fevers and other Salmonella infections. (*f*) Includes scrub, murine and tick typhus. (*g*) Includes leptospiroses, Weil's and para-Weil's disease.

Forristal, Gregory Peter, M.B., B.S., 1947 (Univ. Melbourne), Hobart.

Jarvis, Barry, M.B., B.S., 1939 (Univ. Sydney), Scottsdale.

## Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Swenson, Patricia, M.B., B.S., 1951 (Univ. Sydney), Sydney Hospital, Macquarie Street, Sydney.

Lyttle, Keith Wightman Purvis, M.B., B.S., 1945 (Univ. Sydney), Derby Street, Walcha.

Bull, Richard Stuart, M.B., B.S., 1951 (Univ. Sydney), Broken Hill Hospital, Broken Hill.

Shearman, Rodney Philip, M.B., B.S., 1951 (Univ. Sydney), Royal Prince Alfred Hospital Camperdown.

The undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Brustolin, Nerino, M.B., B.S., 1951 (Univ. Sydney), Sydney Hospital, Macquarie Street, Sydney.

Green, Ruth Helen, M.B., B.S., 1951 (Univ. Sydney), Sydney Hospital, Macquarie Street, Sydney.

Wajnryb, Abraham, registered in accordance with the provisions of section 17 (1) (c) of the *Medical Practitioners Act*, 1938-50, 494 Malabar Road, Maroubra.

## Notice.

### CLINICAL MEETING AT MENTAL HOSPITAL, GLADESVILLE, NEW SOUTH WALES.

A CLINICAL meeting and demonstration of cases will be held in the female admission ward, Mental Hospital, Gladesville, on Thursday, February 22, 1951, at 2.30 p.m. Afternoon tea will be provided. A cordial invitation is extended to all members of the medical profession.

### CRICKET MATCH: DOCTORS VERSUS DENTISTS.

THE annual cricket match between medical men and dentists in New South Wales will be played at the Sydney Cricket Ground on Wednesday, March 7, 1951. Play will commence at 10 a.m. Medical men wishing to be considered for selection should communicate with Dr A. S. Johnson, 185 Macquarie Street, Sydney.

## Honours.

### THE VENERABLE ORDER OF THE HOSPITAL OF ST. JOHN OF JERUSALEM.

THE following medical practitioners have been promoted in or admitted to the Venerable Order of the Hospital of St John of Jerusalem:

*Promoted to the Grade of Commander (Brother).*—Dr. Esca Morris Humphery (New South Wales), Dr Kenneth Barron Fraser (Queensland).

*Promoted to the Grade of Officer (Brother).*—Dr Harold Evans Thomas (New South Wales).

*Admitted in the Grade of Serving Brother.*—Dr Selwyn Graham Nelson (New South Wales), Dr George Joseph Duncan (New South Wales), Dr John Robert Thompson (South Australia), Dr Frederic French Heddle (South Australia), Dr Edward Campbell Pope (Western Australia), Dr Ian Oriel Thorburn (Western Australia).

*Admitted in the Grade of Serving Sister.*—Dr Margherita Maby Freeman (Victoria), Dr Janet Pierson Cooper (Victoria).

## Medical Appointments.

Dr. R. A. Russell has been appointed an honorary clinical assistant to the surgical section of the Royal Adelaide Hospital, Adelaide.

Dr. P. J. Game has been appointed honorary assistant anæsthetist to the orthopædic section of the Royal Adelaide Hospital, Adelaide.

## Diary for the Month.

FEB. 6.—New South Wales Branch, B.M.A.: Organization and Science Committee.

FEB. 7.—Western Australian Branch, B.M.A.: Council Meeting.

FEB. 9.—Queensland Branch, B.M.A.: Council Meeting.

FEB. 13.—New South Wales Branch, B.M.A.: Executive and Finance Committee.

FEB. 20.—New South Wales Branch, B.M.A.: Medical Politics Committee.

## Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

*New South Wales Branch* (Medical Secretary, 135 Macquarie Street, Sydney)—All contract practice appointments in New South Wales.

*Victorian Branch* (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federal Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

*Queensland Branch* (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

*South Australian Branch* (Honorary Secretary, 178 North Terrace, Adelaide): All Lodge appointments in South Australia; all Contract Practice appointments in South Australia; Medical Officer, South Australian Railways.

*Western Australian Branch* (Honorary Secretary, 205 Saint George's Terrace, Perth): Norseman Hospital; all Contract Practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

## Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

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